Respiratory Research Review™

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In this issue:

Abbreviations used in this issue:

aHR = adjusted hazard ratio; **aOR** = adjusted odds ratio;
ARDS = acute respiratory distress syndrome;
ACQ = Asthma Control Questionnaire; **CI** = confidence interval;
COPD = chronic obstructive pulmonary disease;
COVID-19 = coronavirus disease 2019;
FiO_2 = fractional concentration of oxygen in inspired air;
mMRC = modified Medical Research Council;
PaO_2= partial pressure of oxygen;
QOL-B = quality of life bronchiectasis; **RSV** = respiratory syncytial virus.

Welcome to the 83rd issue of Respiratory Research Review.

In this issue we include one of the first published case series of autopsies performed on ten African American people with death attributed to COVID-19. The researchers observed thrombosis and microangiopathy in the small vessels and capillaries of the lungs with associated haemorrhage and diffuse alveolar damage including hyaline membranes. A prospective cohort study assessed prone positioning in non-intubated patients with acute respiratory failure due to COVID-19. The authors found prone positioning was feasible and effective in rapidly ameliorating blood oxygenation in COVID-19-related pneumonia requiring oxygen supplementation. Other interesting findings reported include: oral nitrate supplementation enhances pulmonary rehabilitation in COPD; inhaled aztreonam improves symptoms of cough and sputum production in patients with bronchiectasis; and reduction in all-cause mortality with fluticasone furoate/umeclidinium/vilanterol in patients with chronic obstructive pulmonary disease.

A randomised controlled trial reports on the predictive value of blood eosinophils and exhaled nitric oxide in adults with mild asthma. The concluding article assessed a high-intensity pulmonary rehabilitation programme and found it provides sustained improvements in asthma control, body composition and exercise capacity in obese asthmatics.

I hope you find the research in this issue useful to you in your practice and I look forward to your comments and feedback.

Kind Regards,

Professor Peter Wark

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Air pollution and family related determinants of asthma onset and persistent wheezing in children: Nationwide case-control study

Authors: Holst GJ, et al

Summary: The study cohort, of all Danish children born from 1997 to 2014, were followed for asthma onset and persistent wheezing from age 1 year to 15 years. The authors reported a higher incidence of asthma in children of parents with asthma (adjusted HR 2.29, 95% CI 2.22 to 2.35) and mothers who smoked during pregnancy (1.20, 1.18 to 1.22), whereas a lower incidence was found in children of parents with high educational attainment (0.72, 0.69 to 0.75) and high incomes (0.85, 0.81 to 0.89). Furthermore, exposure to particulate matter ≤2.5 µm (PM 2.5) and ≤10 µm (PM 10) and nitrate was associated with an increased risk of asthma and persistent wheezing.

Comment: This is another large population based epidemiological study that has come out of Denmark where there is excellent access to information in regard to air pollution as well as national patient registries. The researchers investigated the entire population of Danish children born between 1997 and 2014 and followed them in regard to diagnosis of either asthma or persistent wheeze. They found evidence not surprisingly of heightened asthma risk with robust associations between parental asthma, parental education, and maternal smoking during pregnancy and asthma and persistent wheezing. The novelty of this data however was that it also showed a very clear relationship between levels of exposure to PM 2.5 (though not greater particulate sizes) and increased asthma risk. This relationship persisted despite multivariate regression analysis taking into account the other factors that were associated with risk as mentioned. These results once again demonstrate the importance of early life exposure to air pollution and the impact that this has on the development of asthma in developed world countries.

Reference: BMJ. 2020 Aug 19;370:m2791
Abstract

Gefapixant, a P2X3 receptor antagonist, for the treatment of refractory or unexplained chronic cough: A randomised, double-blind, controlled, parallel-group, phase 2b trial

Authors: Smith JA, et al

Summary: Patients were randomly assigned to placebo (n=63), gefapixant 7.5 mg (n=64), gefapixant 20 mg (n=63), or gefapixant 50 mg (n=63) twice daily. At 12 weeks, mean awake cough frequency was 18.2 coughs per hour with placebo, 14.5 coughs per hour with 7.5 mg, 12.0 coughs per hour with 20 mg, and 11.3 coughs per hour with 50 mg gefapixant. Dysgeusia was the most common adverse event, occurring in 5% of patients given placebo, 10% given 7.5 mg gefapixant, 33% given 20 mg gefapixant, and 48% given 50 mg gefapixant.

Comment: Gefapixant is a P2X3 receptor antagonist; purinoceptors are "pain" like peripheral nociceptors that are known to play a role in chronic cough. Chronic refractory cough remains an important cause of chronic disability and results in considerable impairment in quality of life. Despite being such a frequent problem it receives little attention, as it is not perceived as life threatening and studies to look for effective interventions for chronic cough are certainly welcome. This is a phase 2 dose finding study in 253 people with chronic refractory cough who received either placebo or four doses of gefapixant. The average age of patients was in their 60s and the majority were female; not unexpected for a cohort of people with chronic cough. Treatment did lead to an improvement in frequency of cough measured first thing in the morning with the lowest dose demonstrating a 22% reduction in cough frequency and the high dose a 37% reduction. Unfortunately, this was also associated with dysgeusia, or altered taste sensation, a rather unpleasant side effect. It is difficult to gauge the impact that this treatment will have without measures such as improvement in quality of life. A phase three trial in over 700 people is still underway to determine efficacy. The high rate of side effects is concerning as to whether this will be a viable treatment, though such trials are badly needed.

Reference: Lancet Respir Med. 2020 Aug;8(8):775-785
Abstract

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Feasibility and physiological effects of prone positioning in non-intubated patients with acute respiratory failure due to COVID-19 (PRON-COVID): A prospective cohort study

Authors: Coppo A, et al

Summary: This feasibility study investigated the effect on gas exchange of prone positioning in 56 awake, non-intubated patients with COVID-19-related pneumonia. At baseline patients were helped into the prone position, which was maintained for a minimum duration of 3 hours. Clinical data were re-collected 10 min after prone positioning and 1 hour after returning to the supine position. Prone positioning was feasible in 47 patients. The main study outcome was the variation in oxygenation (partial pressure of oxygen [PaO_2]/fractional concentration of oxygen in inspired air [FiO_2]) between baseline and resupination, as an index of pulmonary recruitment. The investigators reported oxygenation substantially improved from supine to prone positioning (PaO_2/FiO_2 ratio 180.5 mm Hg in supine position vs 285.5 mm Hg in prone position; p<0.0001). After resupination, improved oxygenation was maintained in 23 patients; however, this improvement was on average not significant compared with before prone positioning. They also noted patients who maintained increased oxygenation had increased levels of inflammatory markers and shorter time between admission to hospital and prone positioning than did those for whom improved oxygenation was not maintained.

Comment: Prone positioning of patients requiring mechanical ventilation for acute respiratory distress syndrome (ARDS) has been used for some time and is known to reduce complications and improve oxygenation. Until the recent COVID-19 pandemic however it had not been well recognised or discussed outside of this setting. In the early phases of the pandemic with multiple admissions of patients with pneumonia secondary to COVID-19 this started to be explored as an option for treatment.

This is a single prospective cohort study of 56 Italian patients admitted to hospital with COVID-19 and requiring treatment with supplemental oxygen. The patients were proned for a period of at least 3 hours. They accepted patients requiring supplemental oxygen by mask or nasal prongs as well as non-invasive ventilation. There were 47 of the 56 subjects able to complete three hours of prone positioning, while 44 of the subjects required support with non-invasive ventilation though they used this via helmet as opposed to a face or nasal mask. Arterial blood gases were taken 10 minutes after being placed prone and then one hour after returning to a supine position. Oxygenation improved substantially in moving from supine to prone position. When gases were repeated one hour after being supine some improvement still appeared to be present though was no longer statistically significant. Subjects had a mean of two prone positioning cycles with 23 undergoing more than one cycle.

This was not a randomised control study and was simply an observation cohort. The improvement in physiological markers of oxygenation with proning in what is clearly a group with severe hypoxic respiratory failure is certainly an important observation. The addition of prone positioning in this setting was at least feasible though it's not clear how well tolerated it was. Further investigations of this as a modality of treatment should be considered. A randomised control trial would seem to be feasible and is required, though this does not have to be limited to those with COVID-19. It should be considered both inside and outside a critical care setting. This is also an intervention that would need to be adopted with some caution and close observation of patients would be required. Particular care would need to be considered for those who were obese or particularly frail. The national COVID-19 task force has recognised this paper and provides a consensus recommendation that this could be considered. It does however urge that there is limited evidence. I think the best approach would be to encourage this to be in a clinical trial to assess efficacy with clinical outcomes such as requirements for respiratory support, need for intubation or admission to intensive care.

Reference: Lancet Respir Med. 2020 Aug;8(8):765-774
Abstract

Assessing the strength of evidence for a causal effect of respiratory syncytial virus lower respiratory tract infections on subsequent wheezing illness: A systematic review and meta-analysis

Authors: Brunwasser SM, et al

Summary: The meta-analysis included 35 studies evaluating the association between respiratory syncytial virus (RSV) lower respiratory tract infections and subsequent wheezing illness (exposure studies) and 8 studies evaluating the association between RSV immunoprophylaxis and subsequent wheezing illness (immunoprophylaxis studies). The authors reported exposure studies that adjusted for genetic influences yielded a smaller mean adjusted odds ratio (aOR+ 2.45, 95% CI 1.23-4.88) compared with those that did not (4.17, 2.36-7.37); a significant difference (b 0.53, 95% CI 0.04-1.02). Infants who were not protected with RSV immunoprophylaxis had higher odds of subsequent wheezing illness but the effect was not significant (OR+ 1.21, 95% CI 0.73-1.99). The authors noted there was a high risk of confounding bias in the observational studies and a high risk of bias due to missing outcome data.

Comment: Respiratory syncytial virus is still the most common cause of severe wheezing illness in children under the age of 1 year. It is well known that children admitted to hospital as a consequence of RSV are at risk of further episodes of acute wheezing illness and may be at risk for the later development of asthma. It remains controversial whether RSV is the cause of these wheezing illnesses or simply a marker of disease risk. This is a systematic review and meta-analysis of observational studies evaluating the association between RSV infection and subsequent wheezing illness and whether immunoprophylaxis against RSV reduces the risk of later wheezing. While infants who received immunoprophylaxis appeared to have a lower risk, this effect was not significant and it was agreed there was a high risk of both confounding bias by the nature of the observational studies. The conclusion was there was insufficient evidence to justify widespread use of immunoprophylaxis for RSV to prevent early life wheezing illnesses at this stage.

Reference: Lancet Respir Med. 2020 Aug;8(8):795-806
Abstract

Predictive value of blood eosinophils and exhaled nitric oxide in adults with mild asthma: A prespecified subgroup analysis of an open-label, parallel-group, randomised controlled trial

Authors: Pavord ID, et al

Summary: The randomised controlled trial enrolled 675 people with mild asthma receiving only β agonist reliever inhalers from 16 clinical trial units in New Zealand, the UK, Italy, or Australia. Participants were assigned (1:1:1), to receive inhalers to take as-needed salbutamol, maintenance budesonide plus as-needed salbutamol, or as-needed budesonide-formoterol. In this prespecified subgroup analysis, the researchers assessed whether annual exacerbation rates in each treatment group were significantly different depending on levels of blood eosinophil count, exhaled nitric oxide or a composite score of both. Of the patients who received as-needed salbutamol, the proportion of patients having a severe exacerbation increased progressively with increasing blood eosinophil count. There were no significant interactions between blood eosinophil count or exhaled nitric oxide level and the effect of as-needed budesonide-formoterol compared with as-needed salbutamol for either exacerbations or severe exacerbations. In contrast, there were significant interactions between blood eosinophil count subgroups and the effect of maintenance budesonide plus as-needed salbutamol compared with as-needed salbutamol, both for exacerbations (p=0.0006) and severe exacerbations (p=0.0007). Maintenance budesonide plus as-needed salbutamol was more effective than as-needed salbutamol in patients with blood eosinophil counts of 0.3×10^9/L or more, both for exacerbations (rate ratio 0.13) and severe exacerbations (risk odds ratio 0.11). This difference was not seen for blood eosinophil counts of less than 0.15×10^9/L (1.15 for exacerbations and 5.72 for severe exacerbations). It was noted there was no consistent interaction between treatment response and exhaled nitric oxide or the composite score.

Comment: Biomarkers to assess risk of asthma exacerbations have been sought now for some time and would be valuable even in people with mild asthma. This is a re-analysis of a multicentre trial that recruited subjects with mild asthma comparing treatment with regular low dose inhaled corticosteroid to low dose inhaled corticosteroid and formoterol and to as needed salbutamol. They have examined whether blood eosinophil count or exhaled nitric oxide can be used to predict response or risk of exacerbation. The analysis found that even in these subjects with mild asthma an increase in peripheral blood eosinophils was associated with an increased risk of exacerbation with the greatest risk seen in those with a count $\geq 0.3 \times 10^9$/L. Interestingly this was also the group that benefited most in terms of exacerbation reduction when treated with regular low dose budesonide. While those with the blood eosinophil count less than 0.15×10^9/L did not seem to derive a benefit, at least in terms of exacerbation reduction. Even in these subjects with mild asthma evidence of systemic type 2 inflammation with peripheral blood eosinophil predicts exacerbation risk and possibly identifies those who benefit most from the use of inhaled corticosteroids.

Reference: Lancet Respir Med. 2020 Jul;8(7):671-680
Abstract

Pulmonary and cardiac pathology in African American patients with COVID-19: An autopsy series from New Orleans

Authors: Fox SE, et al

Summary: Autopsies were performed on ten African American decedents with cause of death attributed to COVID-19. Pulmonary and cardiac features were examined using immunostains, RNA labelling and electron microscopy on representative sections. The researchers observed thrombosis and microangiopathy in the small vessels and capillaries of the lungs, with associated haemorrhage, that significantly contributed to death. They also found features of diffuse alveolar damage, including hyaline membranes, even in patients who had not been ventilated. Cardiac findings included individual cell necrosis without lymphocytic myocarditis. There was no evidence of secondary pulmonary infection by microorganisms.

Comment: This is one of the first published case series of 10 African American people who died from acute COVID-19 pneumonitis or its complications. Not surprisingly the investigators found evidence of diffuse alveolar damage with proliferative changes and hyaline membrane formation. These findings were typical as to what would be expected in the setting of ARDS. In what would appear however to be unique to COVID-19 they also found evidence of more extensive involvement of pulmonary vessels. There was evidence of extensive haemorrhage; there was evidence of thrombus in small pulmonary arteries and veins. In addition, there was evidence of microthrombi involving the alveolar capillaries but was surrounded by an active perivascular aggregate of lymphocytes suggesting small vessel Inflammation. They went on to investigate cardiac tissue and while they did not find evidence of extensive damage to the myocardium they again found small areas of myocardio necrosis associated with lymph acidic infiltrate. The most notable feature of this study is the obvious involvement of both medium and small vessels in what would be an active inflammatory process associated with COVID-19 that appears to be unique to this virus and has not been seen to the same extent with other severe viral illnesses such as influenza.

Reference: Lancet Respir Med. 2020 Jul;8(7):681-686
Abstract

Reduction in all-cause mortality with fluticasone furoate/umeclidinium/vilanterol in patients with chronic obstructive pulmonary disease

Authors: Lipson DA, et al

Summary: This article is a secondary analysis of efficacy outcomes from the IMPACT (Informing the Pathway of Chronic Obstructive Pulmonary Disease Treatment) trial. Patients with chronic obstructive pulmonary disease (COPD) were randomised 2:2:1 to fluticasone furoate/umeclidinium/vilanterol 100/62.5/25 µg, fluticasone furoate/vilanterol 100/25 µg, or umeclidinium/vilanterol 62.5/25 µg following a run-in on their COPD therapies. Of the intention-to-treat population (n = 10,355), there were 98 (2.36%) deaths on furoate/umeclidinium/vilanterol, 109 (2.64%) on furoate/vilanterol, and 66 (3.19%) on umeclidinium/vilanterol. For furoate/umeclidinium/vilanterol, the hazard ratio for death was 0.72 (P = 0.042) versus umeclidinium/vilanterol and 0.89 (P = 0.387) versus furoate/vilanterol.

Comment: This was a reanalysis of a large multicentre trial of greater than 10,000 people with COPD. The subjects received either so called triple therapy with inhaled fluticasone furate 100 micrograms/vilanterol/umeclidium or fluticasone furate 100 micrograms/vilanterol or vilanterol/umeclidium for 52 weeks. It's important to note that these patients had relatively severe disease with either an FEV1 of less than 50% predicted and one or more exacerbation or had an FEV1 between 50% to 80% predicted with two or more exacerbations that had required oral corticosteroids or at least one exacerbation requiring hospitalisation. This analysis examined the effect of treatment on all-cause mortality. Treatment with fluticasone furate 100 micrograms/vilanterol/umeclidium led to a small but significant reduction in all-cause mortality compared to treatment with dual bronchodilator vilanterol/umeclidium arm of this study. This is the first study to demonstrate this in a prospective way; that inhaled therapy can lead to reduction in mortality. In these COPD people with severe disease, the addition of a medium dose inhaled corticosteroid appears to reduce mortality. Separate studies have suggested that the addition of inhaled corticosteroids do not reduce exacerbations in those with a peripheral blood eosinophil count of < 0.15 by 10^9/L and it is not clear if these results will apply equally to them.

Reference: Am J Respir Crit Care Med. 2020 Jun 15;201(12):1508-1516
Abstract

Intrapleural fibrinolytic therapy versus early medical thoracoscopy for treatment of pleural infection. Randomized controlled clinical trial

Authors: Kheir F, et al

Summary: This prospective, randomised controlled trial included 32 patients with multiloculated pleural infection and empyema who underwent early medical thoracoscopy or intrapleural fibrinolytic therapy for pleural infection. The investigators reported median length of stay after an intervention was 4 days in the intrapleural fibrinolytic therapy arm and 2 days in the medical thoracoscopy arm (P = 0.026). The total length of hospital stay was 6 days in the intrapleural fibrinolytic therapy arm and 3.5 days in medical thoracoscopy arm (P = 0.12). In addition they found no difference in treatment failure, mortality, or adverse events between the treatment groups.

Comment: Acute pleural infections remain an important management problem. This small trial randomised patients to receive early medical thoracoscopy versus insertion of an intercostal catheter with thrombolysis, now regarded as usual care. Treatment failure was the same in both groups but recovery with reduced length of stay was seen in the group that received medical thoracoscopy. These are certainly very promising results and justify further investigation in a larger phase three clinical trial. It reinforces the importance of appropriate and aggressive drainage of pleural infections. It also emphasises the importance of access to interventional procedures such as this, which remains limited to only a few centres with active interventional pulmonary programmes. As the evidence base for these procedures improves they may increasingly be required as standard of care and greater access will need to be considered.

Reference: Ann Am Thorac Soc. 2020 Aug;17(8):958-964
Abstract

Effect of zephyr endobronchial valves on dyspnea, activity levels, and quality of life at one year. Results from a randomized clinical trial

Authors: Dransfield MT, et al

Summary: This was a post hoc analysis of the LIBERATE (Lung Function Improvement after Bronchoscopic Lung Volume Reduction with Pulmonx Endobronchial Valves used in Treatment of Emphysema) trial. The study cohort of 190 patients with severe heterogeneous emphysema and little to no collateral ventilation were randomised 2:1 to the Zephyr Valve or standard of care. The team assessed patient-reported outcomes at 12 months. Patients using the Zephyr Valve achieved statistically significant and clinically meaningful improvements in the St. George's Respiratory Questionnaire, Chronic Obstructive Pulmonary Disease Assessment Test, and the Transitional Dyspnoea Index compared with standard of care. They noted improvements in the St. George's Respiratory Questionnaire were driven by the impacts and activity domains (P < 0.05 and P < 0.001, respectively). Reduction in Chronic Obstructive Pulmonary Disease Assessment Test was through improvements in breathlessness (P < 0.05), energy level (P < 0.05), activities (P < 0.001), and increased confidence when leaving home (P < 0.05). In addition, the Zephyr Valve group significantly improved in the EXAcerbations of Chronic Pulmonary Disease Tool dyspnoea domain.

Comment: This is a re-analysis of data from the "LIBERATE" trial that assessed the effect of the insertion of endobronchial valves in people with heterogeneous emphysema who were quite breathless at baseline, with a median mMRC (modified Medical Research Council) dyspnoea score of 2.4. At 12 months these patients still demonstrated both statistically significant improvements in their symptoms of breathlessness and as a result increased activity levels with the intervention. These results did correlate with the physiological improvements in lung function. These people of course remain a highly selected group with COPD, characterised by severe airflow limitation, with impaired dynamic hyperinflation and heterogeneous emphysema. However, phase improvements also need to be seen as being additional to medical therapy and certainly demonstrate a substantial and long-lasting improvement. This justifies considering this as a treatment in properly selected patients. Greater access to this as a treatment should certainly be now considered in the Australian health care context where this still does not receive specific support in many jurisdictions.

Reference: Ann Am Thorac Soc. 2020 Jul;17(7):829-838
Abstract

Oral nitrate supplementation to enhance pulmonary rehabilitation in COPD: ON-EPIC a multicentre, double-blind, placebo-controlled, randomised parallel group study

Authors: Pavitt MJ, et al

Summary: This study, performed at four UK centres, enrolled adults with grade II-IV COPD and MRC dyspnoea score 3-5 or functional limitation. Participants were randomly assigned to either nitrate-rich beetroot juice (n = 57), or placebo (n = 65), consumed 3 hours prior to undertaking each pulmonary rehabilitation session (twice weekly 8-week programme). Exercise capacity increased more with nitrate-rich beetroot juice than placebo with median change in incremental shuttle walk test distance +60 m versus +30 m; estimated treatment effect 30 m (p=0.027). Nitrate-rich beetroot juice also impacted on systolic blood pressure: treatment group -5.0 mmHg versus control +6.0 mmHg; estimated treatment effect -7 mmHg (p<0.0005).

Comment: Pulmonary rehabilitation is an effective treatment for people with COPD. Enhancing its effect to further maximise its value would also be clearly worthwhile. Nitric oxide is a regulator of skeletal muscle blood flow and improves contractility and presumably muscle function. Previous research has shown that supplementation of nitrates to the diet improves exercise capacity. The investigators proposed that dietary nitrate supplementation prior to each session of a pulmonary rehabilitation programme would enhance the exercise capacity of participants. This multicentre trial recruited 165 participants, 78 were randomised to a nitrate rich beetroot juice supplement and 87 to placebo. The intervention group demonstrated improved exercise capacity in terms of the incremental shuttle walk test with the supplement arm achieving 60 metres increase compared to 30 metres in the placebo arm. There were no differences seen in the MRC dyspnoea score or the CAT score. The dietary supplementation was also well tolerated.

This is certainly an interesting concept and a promising result. While this has translated to a significant short-term improvement in exercise capacity the real benefit would be if it's sustained over a better training programme or assisted in maintaining better levels of activity in the long run. In both of these cases further investigations will be required to determine whether this will be the case.

Reference: Thorax. 2020 Jul;75(7):547-555
Abstract

Inhaled aztreonam improves symptoms of cough and sputum production in patients with bronchiectasis: A post hoc analysis of the AIR-BX studies

Authors: Crichton ML, et al

Summary: The investigators conducted a post hoc analysis of the AIR-BX1 studies and two trials of inhaled aztreonam versus placebo in bronchiectasis. Items from the quality of life bronchiectasis (QOL-B) respiratory symptom scale were analysed, representing severity of nine distinct symptoms. They evaluated changes in symptoms with treatment versus placebo from baseline to end of first on-treatment cycle in addition to changes across the full 16-week trial. Aztreonam improved cough (difference 0.22, p=0.002), sputum production (0.30, p<0.0001) and sputum colour (0.29, p<0.0001) versus placebo equating to a 20% improvement in cough and 25% improvement in sputum production and colour. They also observed similar results for cough, sputum production and sputum purulence across the trial duration (all p<0.05).

Comment: Effective treatments are needed for people with bronchiectasis but many of the previous trials have failed to show improved outcomes leaving patients with few clear treatment options. Criticisms of these trials have included they have not selected the correct patients, do not use accurate outcomes and there are relatively few outcomes that are specific or clinically meaningful for people with bronchiectasis. The QOL-B is the only disease-specific tool that has been tested in multiple randomised trials and the investigators have used this to re-examine the effects of one of these clinical trials, looking at the impact of inhaled aztreonam on these patients. Not only did they demonstrate that treatment with inhaled aztreonam improved symptoms of cough and sputum production, they also demonstrated that people with these symptoms were the most likely to respond. When taken into account that these trials have also previously shown inhaled antibiotics can reduce airway inflammation and improve microbiological endpoints these are important outcomes to measure and to design clinical trials around.

Reference: Eur Respir J. 2020 Jul 16;56(1):2000608
Abstract

Short-term and long-term effect of a high-intensity pulmonary rehabilitation programme in obese patients with asthma: A randomised controlled trial

Authors: Türk Y, et al

Summary: The study cohort comprised of 34 patients with obesity (body mass index (BMI) ≥30 kg.m^{-2}) and suboptimal controlled asthma (Asthma Control Questionnaire (ACQ) ≥0.75). Patients were randomly assigned to a 3-month pulmonary rehabilitation programme (n = 14), pulmonary rehabilitation programme with the use of an internet based self-management support programme (n = 9) or usual care (n = 11). The pulmonary rehabilitation programme included high-intensity interval training, nutritional intervention and psychological group sessions, while the usual care group were advised to lose weight and to exercise. After 3 months patients in the pulmonary rehabilitation programme only group had a significant reduction in BMI and significant improvements in asthma control, exercise capacity and aerobic capacity, compared with patients in the usual care group. These improvements persisted during 12 months of follow-up. No difference in ACQ between pulmonary rehabilitation with self-management support programme and pulmonary rehabilitation programme only groups was observed. However, patients in the pulmonary rehabilitation with self-management support programme had a significantly lower BMI after 12 months compared with patients in the pulmonary rehabilitation programme only group.

Comment: While improvements to the care of people with severe asthma have occurred, particularly with the use of monoclonal antibodies that have been shown to reduce exacerbation frequency and improve asthma control, those with severe asthma still have a very high burden of illness. This small but interesting Dutch study took a group of obese people with asthma and ongoing poor control and randomised them to receive a training programme with pulmonary rehabilitation that included high intensity training, together with nutritional advice and support, a less intense programme with pulmonary rehabilitation and self-management and then usual care that was simply advice to lose weight and exercise. Well the trial was very small, with only 34 individuals, the intense programme demonstrated a reduction in BMI as well as improvements in asthma control and exercise capacity after the three months of the programme and these persisted up to 12 months. These programmes remain quite promising but do need to be replicated in larger groups and shown to be just as effective as well as being able to sustain these positive outcomes.

Reference: Eur Respir J. 2020 Jul 2;56(1):1901820
Abstract

Independent commentary by Conjoint Professor Peter Wark

Prof Peter Wark is a senior staff specialist in Respiratory and Sleep Medicine at John Hunter Hospital, Newcastle, Australia and a conjoint Professor with the University of Newcastle. In addition, he is a senior investigator with the Priority Research Centre for Healthy Lungs and the Vaccines Immunology Viruses and Asthma research group at the Hunter Medical Research Institute. He is also a chief investigator in the National Health and Medical Research Council Centre of Excellence in Severe Asthma. His research interests are in the area of infection and the impact this has on inflammatory airways disease, with a particular interest in viral respiratory infections and acute exacerbations of chronic airways disease.

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