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Assessing the impact of diet, exercise and the combination of the two as a treatment for OSA: A systematic review and meta-analysis.

Edwards, BA, Bristow, C, O'Driscoll, DM, et al.

Respirology. 2019; 24: 740– 751.

https://doi.org/10.1111/resp.13580

ABSTRACT

This study aimed to provide an updated systematic review and meta-analysis of randomized controlled trials (RCT) investigating the effectiveness of lifestyle interventions on weight loss and the impact on the severity of obstructive sleep apnoea (OSA). A systematic search of five databases between 1980 and May 2018 was used to identify all RCT which employed a lifestyle intervention (i.e. diet-only, exercise-only or combination of the two) aiming to reduce the severity of OSA (assessed using the apnoea–hypopnoea index (AHI)). Random-effects meta-analyses followed by meta-regression were conducted. Ten RCT involving 702 participants (Intervention group: n = 354; Control group: n = 348) were assessed in two meta-analyses. The weighted mean difference in AHI (−8.09 events/h, 95% CI: −11.94 to −4.25) and body mass index (BMI, −2.41 kg/m^2, 95% CI: −4.09 to −0.73) both significantly favoured lifestyle interventions over control arms. Subgroup analyses demonstrated that all interventions were associated with reductions in the AHI, but only the diet-only interventions were associated with a significant reduction in BMI. No association was found between the reduction in AHI or BMI and the length of the intervention, or with baseline AHI and BMI levels. All lifestyle interventions investigated appear effective for improving OSA severity and should be an essential component of treatment for OSA. Future research should be directed towards identifying subgroups likely to reap greater treatment benefits as well as other therapeutic benefits provided by these interventions.

Indacaterol/glycopyrronium versus tiotropium or glycopyrronium in long-acting bronchodilator-naïve COPD patients: A pooled analysis.

Muro, S, Yoshisue, H, Kostikas, K, Olsson, P, Gupta, P, Wedzicha, JA.

Respirology. 2019; 1– 8.

https://doi.org/10.1111/resp.13651

ABSTRACT

Background and objective

Indacaterol/glycopyrronium (IND/GLY) 110/50 μg once daily (q.d.) has demonstrated greater improvements in lung function, patient-reported outcomes and lower exacerbation rates versus mono long-acting muscarinic antagonists (LAMA) in chronic obstructive pulmonary disease (COPD) patients. However, data are limited on initial treatment with IND/GLY 110/50 μg q.d. versus mono LAMA in COPD patients, not previously on maintenance treatment with long-acting bronchodilators (LABD).

Methods

A pooled analysis of ARISE, SHINE and SPARK trials was conducted to evaluate the efficacy of IND/GLY 110/50 μg q.d. versus open-label (OL) tiotropium (TIO) 18 μg q.d. and GLY 50 μg q.d. in COPD patients, not on maintenance treatment with LABD at study entry (LABD-naïve). Efficacy was assessed after 24/26 weeks of treatment.

Results

In total, 998 LABD-naïve patients were included (IND/GLY: 353; OL TIO: 328; GLY: 317). Patients treated with IND/GLY 110/50 μg q.d. experienced greater improvements in trough forced expiratory volume in 1 s (FEV_1) versus OL TIO 18 μg q.d. (least squares mean treatment difference (Δ): 0.086 L) and GLY 50 μg q.d. (Δ: 0.080 L) after 24/26 weeks. Improvements in electronic diary (eDiary) symptom scores, transition dyspnoea index (TDI) focal score, St George's Respiratory Questionnaire (SGRQ) total score and rescue medication use were also greater with IND/GLY versus OL TIO and GLY. Greater proportion of patients achieved minimal clinically important difference in trough FEV_1, TDI and SGRQ with IND/GLY versus OL TIO and GLY.

Conclusion

LABD-naïve patients treated with IND/GLY 110/50 μg q.d. achieved improvements in lung function, daily symptoms, dyspnoea, health-related quality of life and rescue medication use versus those who received single LAMA.

Real-life effectiveness of inhaler device switch from dry powder inhalers to pressurized metred-dose inhalers in patients with asthma treated with ICS/LABA.

Park, H-S, Yoon, D, Lee, HY, et al.

Respirology. 2019; 24: 972– 979.

https://doi.org/10.1111/resp.13559

ABSTRACT

Background and objective

Mixed inhaler device use for asthma is associated with worse inhaler technique and outcomes. Given that relievers are commonly prescribed as pressurized metred-dose inhalers (pMDI), changing preventers from dry powder inhalers (DPI) to pMDI may improve asthma outcomes. This study aimed to assess the persistence and effectiveness of switching from DPI to pMDI for inhaled corticosteroid and long-acting β_2-agonist combination therapy (ICS/LABA).

Methods

This was a historical cohort study using Ajou University Hospital (Korea) patient records. Persistence of switch was defined as receiving ≥1 pMDI and no DPI after the switch. Effectiveness of switch was assessed as the proportion without severe asthma exacerbation and the proportion achieving risk domain asthma control (RDAC; no asthma-related hospitalization, antibiotics without upper respiratory diagnosis or acute course of oral corticosteroids) and overall asthma control (OAC; RDAC and ≤ 200 μg salbutamol/≤500 μg terbutaline average daily dose) comparing 1 year after and before the switch.

Results

Within 85 patients who switched from DPI to pMDI and persisted for a year, higher proportion were free from asthma exacerbation after the switch (mean difference in proportion = 0.129, 95% CI: 0.038–0.220). Switching to pMDI was also associated with better RDAC (75.3% vs 57.7%, P = 0.001) and OAC (57.7% vs 45.9%, P = 0.021). From the entire 117 patients who switched to fixed-dose combination (FDC)/ICS LABA pMDI, 76.1% (95% CI: 69.0–100.0%) patients persisted in the following 6 months.

Conclusion

Switching to and persisting with pMDI was associated with decreased asthma exacerbations and improved asthma control. The majority of patients persisted with the switch to pMDI for ICS/LABA treatment.

Efficacy of corticosteroid and intravenous cyclophosphamide in acute exacerbation of idiopathic pulmonary fibrosis: A propensity score-matched analysis.

Hozumi, H, Hasegawa, H, Miyashita, K, et al.

Respirology. 2019; 24: 792– 798.

https://doi.org/10.1111/resp.13506

ABSTRACT

Background and objective

Acute exacerbation (AE) is a leading cause of death in patients with idiopathic pulmonary fibrosis (IPF). Although optimal treatment for AE-IPF remains unclear, high-dose corticosteroids (CS) with/without immunosuppressants, including intravenous cyclophosphamide (IVCY), are often used as empirical therapy. However, the survival benefit of adding IVCY to CS therapy is unknown. We investigated the efficacy of this therapy in patients with AE-IPF.

Methods

Overall, 102 consecutive patients with IPF with a first idiopathic AE were included. Post-AE survival rates and treatment safety were retrospectively assessed. Efficacy of CS + IVCY therapy for the first AE was compared with that of CS monotherapy using a propensity score-matched analysis.

Results

The post-AE 90-day survival rate of the entire cohort was 64.7%. On the basis of the propensity scores, 26 matched patient pairs were made. Characteristics of matched patients with AE-IPF treated with CS (matched CS group) and those with CS + IVCY (matched CS + IVCY group) were well balanced. No significant between-group differences were observed in post-AE 90-day survival rates (84.6% vs 76.9%; $P = 0.70$), cumulative survival rates ($P = 0.57$ by log-rank test) or incidence of adverse events ≥ CTCAE (Common Terminology Criteria for Adverse Events) v5.0 grade 3 (61.5% vs 65.4%; $P = 1.00$).

Conclusion

The propensity score-matched analysis demonstrated that compared with CS monotherapy, CS + IVCY therapy did not significantly improve post-AE survival in patients with AE-IPF. Further studies are warranted to assess the efficacy of CS + IVCY therapy for AE-IPF.

Molecular breath analysis supports altered amino acid metabolism in idiopathic pulmonary fibrosis.

Gaugg, MT, Engler, A, Bregy, L, et al.

Respirology. 2019; 24: 437– 444.

https://doi.org/10.1111/resp.13465

ABSTRACT

Background and objective

Diagnosis of idiopathic pulmonary fibrosis (IPF) is complex and its pathogenesis is poorly understood. Recent findings indicate elevated levels of proline and other amino acids in lung tissue of IPF patients which may also be of diagnostic value. Following these findings, we hypothesized that such altered metabolic profiles would be mirrored in exhaled breath and could therefore be captured non-invasively in real time.

Methods

We aimed to validate these results using real-time exhaled breath analysis by secondary electrospray ionization-mass spectrometry, which can provide a non-invasive, painless and fast insight into the metabolism. Breath analysis was performed in a matched 1:1 case–control study involving 21 patients with IPF and 21 control subjects.

Results

We found significantly ($P < 0.05$) elevated levels of proline, 4-hydroxyproline, alanine, valine, leucine/isoleucine and allysine in breath of IPF patients, whereas pyroglutamic acid and phenylalanine did not show significant differences. This coincides with the amino acid's abundance in pulmonary tissue indicating that our observations reflect progressing fibrosis. In addition, amino acid levels correlated across subjects, further supporting a common underlying pathway. We were able to obtain a cross-validated area under the curve of 0.86, suggesting that these increased amino acid levels in exhaled breath have the potential to be used as biomarkers for IPF.

Conclusion

We could validate previous findings of elevated lung tissue amino acid levels in IPF and show that online breath analysis might be a practical tool for a rapid screening for IPF.

Quantitative CT-derived vessel metrics in idiopathic pulmonary fibrosis: A structure–function study.

Jacob, J, Pienn, M, Payer, C, et al.

Respirology. 2019; 24: 445– 452.

https://doi.org/10.1111/resp.13485

ABSTRACT

Background and objective

This study aimed to investigate whether quantitative lung vessel morphology determined by a new fully automated algorithm is associated with functional indices in idiopathic pulmonary fibrosis (IPF).

Methods

A total of 152 IPF patients had vessel volume, density, tortuosity and heterogeneity quantified from computed tomography (CT) images by a fully automated algorithm. Separate quantitation of vessel metrics in pulmonary arteries and veins was performed in 106 patients. Results were evaluated against readouts from lung function tests.

Results

Normalized vessel volume expressed as a percentage of total lung volume was moderately correlated with functional indices on univariable linear regression analysis: forced vital capacity ($R^2 = 0.27$, $P < 1 \times 10^{-6}$), diffusion capacity for carbon monoxide (DL_{CO}; $R^2 = 0.12$, $P = 3 \times 10^{-5}$), total lung capacity (TLC; $R^2 = 0.45$, $P < 1 \times 10^{-6}$) and composite physiologic index (CPI; $R^2 = 0.28$, $P < 1 \times 10^{-6}$). Normalized vessel volume was correlated with vessel density but not with vessel heterogeneity. Quantitatively derived vessel metrics (and artery and vein subdivision scores) were not significantly linked with the transfer factor for carbon monoxide (K_{CO}), and only weakly with DL_{CO}.
On multivariable linear regression analysis, normalized vessel volume and vessel heterogeneity were independently linked with DL_{CO}, TLC and CPI indicating that they capture different aspects of lung damage. Artery–vein separation provided no additional information beyond that captured in the whole vasculature.

Conclusion

Our study confirms previous observations of links between vessel volume and functional measures of disease severity in IPF using a new vessel quantitation tool. Additionally, the new tool shows independent linkages of normalized vessel volume and vessel heterogeneity with functional indices. Quantitative vessel metrics do not appear to reflect vasculopathic damage in IPF.

Nasal high-flow therapy compared with non-invasive ventilation in COPD patients with chronic respiratory failure: A randomized controlled cross-over trial.

McKinstry, S, Singer, J, Baarsma, JP, Weatherall, M, Beasley, R, Fingleton, J.

Respirology. 2019; 24: 1081– 1087.

https://doi.org/10.1111/resp.13575

ABSTRACT

Background and objective

Non-invasive ventilation (NIV) is part of the standard of care for hypercapnic respiratory failure secondary to COPD, but may be poorly tolerated. Preliminary evidence suggests nasal high-flow (NHF) therapy may improve hypercapnia in COPD and be well tolerated. We compared NHF and NIV in people with COPD and chronic hypercapnic respiratory failure.

Methods

Single-blind randomized controlled two-way cross-over single-centre trial was conducted in New Zealand. Twenty-four participants with stable hypercapnic COPD received: NHF at 45 L/min and NIV at 15/4 cm H_2O, each for 60 min with a 15-min washout in between. The primary outcome was transcutaneous partial pressure of carbon dioxide ($PtCO_2$) at 60 min, adjusted for baseline.

Results

NIV reduced the $PtCO_2$ more than NHF (mean (SD) at 60 min by −5.3 (5.0) vs −2.5 (3.5) mm Hg; difference: −2.8 (−5.0 to −0.5) P = 0.021). Difference across all time points was −2.5 mm Hg (95% CI −4.5 to −0.5, P = 0.016). There was no significant difference in the proportion of participants with a reduction of $PtCO_2 \geq 4$ or ≥ 8 mm Hg. Participants rated NHF significantly better for ease of application, comfort and fit.

Conclusion

In stable COPD patients with chronic hypercapnia, NIV resulted in a greater reduction in $PtCO_2$ compared with NHF, which was of uncertain clinical significance. NHF was better tolerated than NIV and may be a therapeutic option for some people with hypercapnic respiratory failure.Clinical Trial Registration: ACTRN12616001701415 at www.anzctr.org.au

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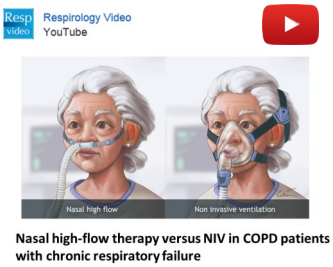
https://youtu.be/Co-quvyLW8M



Nasal high-flow therapy versus NIV in COPD patients with chronic respiratory failure

Recombinant thrombomodulin for acute exacerbation in idiopathic interstitial pneumonias.

Arai, T, Kida, H, Ogata, Y, et al.

Respirology. 2019; 24: 658– 666.

https://doi.org/10.1111/resp.13514

ABSTRACT

Background and objective

Acute exacerbation (AE) in idiopathic pulmonary fibrosis (IPF) or other idiopathic interstitial pneumonias (IIP) is a poor prognostic event despite conventional therapy with corticosteroids and/or immunosuppressants. We aimed to evaluate the efficacy and safety of recombinant human soluble thrombomodulin (rhTM) for AE-IIP.

Methods

For this prospective single-arm open-label multicentre cohort study, we retrospectively registered 61 cases of AE-IIP treated with conventional therapy between 2011 and 2013 (control arm), and prospectively enrolled 39 cases of AE-IIP treated with conventional therapy and rhTM (380 U/kg/day for 6 days) between 2014 and 2016 (rhTM arm). To reduce potential confounding in treatment comparisons, an adjusted mortality analysis for 90-day survival was conducted with weighted Cox proportional hazards regression models using inverse probability of treatment weighting. Weights were derived from propensity scores estimated using a multivariable logistic regression analysis including potential confounders.

Results

The 90-day survival rates of AE-IIP patients treated with/without rhTM were 66.7% (26/39) and 47.5% (29/61), respectively. After adjusting for imbalances, rhTM therapy was significantly associated with reduced mortality (adjusted hazard ratio (HR): 0.453; 95% CI: 0.237–0.864; P = 0.0163). The frequencies of adverse events with/without rhTM were 17.9% (7/39) and 19.7% (12/61), which were similar in both arms (P = 1.0). Two bleeding-related adverse events occurred in the rhTM arm.

Conclusion

Safety and efficacy were observed for rhTM treatment of AE-IIP. A future randomized controlled trial is required to draw final conclusions.

Therapeutic burden in interstitial lung disease: Lessons to learn.

Khor, YH, Glaspole, I, Goh, NSL.

Respirology. 2019; 24: 566– 571.

https://doi.org/10.1111/resp.13480

ABSTRACT

Background and objective

Patients with interstitial lung disease (ILD) are often prescribed disease-targeted and symptomatic therapies, both of which can cause significant treatment burden due to polypharmacy and drug–disease interactions. This study aimed to evaluate medication regimen complexity before and after introduction of ILD-specific therapies. Potential drug–disease interactions were evaluated for patients who were prescribed prednisolone.

Methods

In this study, 214 patients with ILD were assessed for demographic information, co-morbidities and medication use. Medication lists were reviewed prior to and after the introduction of ILD-specific therapies. Complexity of treatment regimen was examined using the validated Medication Regimen Complexity Index (MRCI).

Results

Of the 214 patients, 75 had idiopathic pulmonary fibrosis (IPF) while the rest had inflammatory ILD (chronic hypersensitivity pneumonitis: 45; connective tissue disease-related ILD: 41). Polypharmacy was common at baseline (IPF: 51%, inflammatory ILD: 63%). Following introduction of ILD-specific therapies, median total MRCI scores significantly increased from 8 (interquartile range (IQR) = 8–15) to 22.5 (17.5–27.5) and 14.5 (8.5–21) to 21.5 (16–30) for IPF and inflammatory ILD groups, respectively ($P < 0.0001$ for both). Complex dosing instructions contributed the most to total MRCI scores for ILD-specific therapies. Among patients receiving prednisolone ($n = 113$), 88% had ≥1 co-morbidity which may be impacted. Common co-morbidities included gastrointestinal diseases (56%), obesity (37%), osteoporosis (24%) and diabetes mellitus (18%).

Conclusion

Polypharmacy and complex medication regimen are common in patients with ILD of different aetiologies. There is a high frequency of potential drug–disease interactions among patients who are prescribed systemic corticosteroids. These findings highlight the need for careful evaluation of the impact of therapeutic complexity and burden in patients with ILD.

Idiopathic chronic productive cough and response to open-label macrolide therapy: An observational study.

Martin, MJ, Lee, H, Clayton, C, et al.

Respirology. 2019; 24: 558– 565.

https://doi.org/10.1111/resp.13483

Abstract

Background and objective

Adult patients with chronic productive cough of unknown cause are commonly seen in respiratory clinics. We have previously described a subgroup of these patients who have a short-lived response to standard antibiotic treatment but a prolonged response to 3 months of low-dose azithromycin therapy.

Methods

This observational study describes the physiological, radiological and pathological features of this patient cohort along with their response to a 12-week open-label trial of 250 mg azithromycin thrice weekly.

Results

A total of 30 subjects with a mean age of 57 were recruited. The majority demonstrated airway dilatation on high-resolution computed tomography (HRCT) scan without evidence of established bronchiectasis ($n = 21$) and non-specific chronic inflammatory changes on bronchial biopsy ($n = 15/17$). Twenty-nine subjects completed 3 months of azithromycin with a significant improvement in median Leicester Cough Questionnaire (LCQ) score (−6.3 points, $P < 0.00001$), reduction in median 24-h sputum volume (−5.8 mL, $P = 0.0003$) and improvement in sputum colour ($P = 0.003$). Patients responsive to azithromycin ($n = 22$) demonstrated neutrophilic or paucigranulocytic airway inflammation, whereas five subjects with eosinophilic airways inflammation did not respond symptomatically to azithromycin.

Conclusion

We describe a cohort of patients with chronic productive cough not adequately described by existing disease labels whose symptoms responded well to low-dose azithromycin. Many of the features are similar to the paediatric condition protracted bacterial bronchitis.

APSR Respiratory Updates is an initiative of the APSR Education Committee

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