Journal club

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AS-NEEDED ICS-LABA IN MILD ASTHMA: REDUCES SHORT-TERM RISK OF SEVERE EXACERBATION AFTER A SINGLE DAY OF INCREASED USE

The cornerstone of the management of mild asthma has been regular inhaled corticosteroids (ICS) but there is increasing interest in the use of a single combined ICS long-acting β-agonist (LABA) to reduce exacerbation risk. O'Byrne *et al* (*Lancet Respir Med* 2020; doi: 10.1016/S2213-2600(20)30416-1) performed a post-hoc analysis of the SYGMA 1 study to assess short-term risk of severe exacerbations after a single day of increased use (>2) of short-acting β-agonist (SABA). In the double-blind SYGMA 1 trial, 3849 patients with mild asthma were randomised to one of the three arms: as-needed SABA, as-needed ICS-LABA or ICS maintenance. They investigated the frequency of SABA use and the risk of severe exacerbation in the 21 days after first use of >2 inhalations in a single day. Severe exacerbation was defined as use of systemic corticosteroids for ≥3 days, asthma requiring emergency room visit or inpatient admission. Patients in all three treatment arms used no reliever on 70.0%–77.5% of study days. Significantly fewer patients in both as-needed ICS-LABA and ICS maintenance groups used more than two reliever inhalations in a single day than patients in the as-needed SABA group (p=0.0002). When a single day of >2 reliever inhalations were required, use of regular ICS maintenance therapy reduced risk of a severe exacerbation in the next 21 days versus SABA alone (HR 0.39; 95% CI 0·19 to 0·79; p=0·0091). Use of as-needed ICS-LABA was equally effective in protecting against severe exacerbation (HR 0.27; 95% CI 0.12 to 0.58; p=0.0008). This trial provides evidence that in the context of mild asthma with infrequent use of relievers, as-needed ICS-LABA might be a viable alternative to rescue SABA providing protection against severe exacerbations that is non-inferior to daily ICS therapy.

SUBPLEURAL LUNG LESIONS: USE OF TRANSTHORACIC SHEAR-WAVE ULTRASOUND ELASTOGRAPHY TO PREDICT MALIGNANCY

Lung malignancy can present as non-resolving pneumonia resulting in delay in diagnosis and treatment due to the lack of reliable and safe diagnostic modality. Kuo *et al* (*Eur Respir J* 2020; doi: 10.1183/13993003.02347–2020) assessed the application of transthoracic 2D shear-wave ultrasound elastography in differentiating malignant from benign subpleural lung lesions. The authors retrospectively analysed 121 patients in the derivation cohort to determine the optimal cut-off point and prospectively enroled 233 patients over 2 years in the validation cohort. All 354 patients had either a biopsy, microbiological studies or clinical follow-up to reach a final diagnosis of benign or malignant lung lesions. The elasticity cut-off point of 65 kPa was derived from the derivation cohort to differentiate benign from malignant lesions with a maximal Youden index 0.60 (sensitivity 89.7%, specificity 70.6%, accuracy 84.3%, p<0.001). The diagnostic performance was maintained in the validation cohort with Youden index 0.65 and accuracy 86.7%. Elasticity of >65 kPa was an independent predictor of lung malignancy after adjusting for age, sex, body mass index and lung lesion size. The majority of benign lesions were bacterial and fungal pneumonia with the most common lung malignancy adenocarcinoma. Transthoracic shear-wave elastography provides objective information of characteristic of subpleural lesions and represents a reliable modality to predict lung malignancy.

NON-INVASIVE VENTILATION IN PRETERM INFANTS: USE OF CANNULAS WITH LONG AND NARROW TUBING VERSUS SHORT BINASAL PRONGS

Cannulas with long and narrow tubing (CLNT) are increasingly used to provide non-invasive ventilation (NIV) in preterm infants, however, there is insufficient data available on the clinical efficacy compared with short binasal prongs and masks (SPM). Hochwald *et al* (*JAMA Pediatrics* November 2020; doi: 10.1001/jamapediatrics.2020.3579) conducted a randomised, dual-centre study evaluating if CLNT is non-inferior to SPM using an intention-to-treat analysis. Preterm infants (24 to 33 weeks and 6 days' gestation) requiring NIV were randomised to receive either CLNT (n=83) or SPM (n=83). A standard protocol was adopted to optimise respiratory support and tube size in both treatment groups. CLNT was non-inferior to SPM with regard to the need for intubation within 72 hours of initiation of NIV (14% vs 18%; 95% CI −14.8 to 7.6; p=0.53). A subgroup analysis by birth weight (<1250 g), although underpowered because of a small sample size, demonstrated non-inferiority of CLNT when compared with SPM (17% vs 23%; 95% CI −22.9 to 11.3; p=0.51). Moderate-to-severe nasal traumas were significantly higher in the SPM group compared with CLNT (17% vs 5%; 95% CI 0.02 to 0.22; p=0.01). The study supports clinicians to use CLNT in this patient group to deliver similar efficacy and improved comfort.

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COCHRANE NEWSFLASH

Corrector therapies in CF: improved outcomes with more drugs

Patients with cystic fibrosis (CF) have a defect in the CF transmembrane conductance regulator (CFTR). Therapies correcting this proteins function offer potential disease-modifying impact in CF. A newly published Cochrane Review https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD010966.pub3/full of CFTR corrector therapies includes evidence from eight randomised controlled trials (RCTs) looking at five different monotherapies (344 participants), six RCTs of two dual-therapies lumacaftor–ivacaftor and tezacaftor–ivacaftor (1840 participants) and five RCTs of two triple-therapies elexacaftor–tezacaftor–ivacaftor and VX-659-tezacaftor-ivacaftor (775 participants). In most RCTs (n=14) participants had F508del/F508del genotypes, in three RCTs F508del/minimal function (MF) and in two RCTs both F508del/F508del and F508del/MF genotypes. The authors found insufficient evidence that any corrector monotherapy has clinically important effects in F508del/F508del. Dual therapy resulted in improvements in quality of life and respiratory function with lower pulmonary exacerbation rates compared with placebo. Lumacaftor–ivacaftor was associated with some adverse effects that were not observed with tezacaftor–ivacaftor, but data are lacking for tezacaftor–ivacaftor in children under 12 years. Triple combination with elexacaftor in patents with one or two F508del variants saw greater improvements in important clinical outcomes than dual therapies with no safety concerns identified, but further RCTs are required in children under 12 years and those with more severe respiratory function. High-quality evidence led the authors to conclude that elexacaftor–tezacaftor–ivacaftor triple-therapy should be the standard of care for people with CF with one or two F508del variants aged 12 years or older.

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