Cochrane Airways Group News
July 2012

Review group news from Emma Welsh

We’ve been very busy this year working with teams and publishing loads of reviews this year – you can find out what we published at the end of the newsletter! Particular highlights have been the high percentage of new reviews with summary of findings tables. We’ve had success in creating skeleton summary of findings tables and passing them back to author teams – who are the experts on their reviews – for fine-tuning and fleshing out.

Welcome to a new editor: We have welcomed Sally Spencer as an editor this year. Sally is the Associate Director of Clinical Research for the Clinical Research Hub in the School of Health of Medicine at the University of Lancaster. Sally brings her experience in building cross-sectoral research partnerships to underpin high quality clinical research and is known for her work on the St George’s Respiratory Questionnaire for COPD.

Vacancy at the Cochrane Airways Group: this week we are congratulating Charlotta Karner, our research assistant, on her new job at the BMJ. We are in the process of getting a vacancy advertised through St George’s University – the position will be advertised here (http://airways.cochrane.org/job-announcements) in the next week. Please check back if you are interested in working with us on systematic reviews of COPD on a full time basis for a year here at St George’s in London. Projected closing date is the 7th September 2012.

European Society Meeting, Vienna, Austria: We are running a Cochrane session at the ERS in Vienna on the 2nd September and the session has been selected as a highlight! Two of our editors are speaking in the session. Francine Ducharme will discuss what’s new in childhood asthma:

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The Airways Group is one of 52 Review Groups in The Cochrane Collaboration. Our reviews are concerned with treatments for asthma, COPD, sleep apnoea, pulmonary hypertension, chronic cough and bronchiectasis. We maintain a specialized register of controlled trials in chronic airways disease.
myths and realities and Milo Puhan will be speaking about translational paths for clinical trials to medical decision making for COPD. There will also be a talk from another Cochrane working in the Acute Respiratory infections Group on his controversial review on neuramidase inhibitors for preventing and treating influenza and Antoine Magnan will present a fresh look at a suite of Emergency Medicine reviews that Steve Milan has updated here at the Editorial base in collaboration with clinicians based in Canada and the UK. The chairs, Chris Cates and John White, warmly invite you to attend and hope to see some of you there – do come and say hello at the end!

Cochrane Colloquium 2012: The Colloquium is in New Zealand this year, 30 September – 3 October – full details here http://colloquium.cochrane.org either come and say hi at meet the entities – I’ll be all on my own! – or email me to arrange a time just to say hi or discuss your review.

Visitors: We have had several local reviewers visit us for hands on help with their reviews. We have found it is possible to enter all the data into a review and for authors to get a good grounding in how to use RevMan and to ask any questions about statistics or how to write up their results and discussion sections. We would encourage any authors visiting London to drop by to meet up – we can make a laptop available to you to work on your review and meeting face-to-face can really help speed things along. If you can’t call by but would like a guided tour of RevMan over the Skype, email me to arrange a time – I can share my screen with you using Skype and help you start entering data if you are stuck with RevMan.

Hot tips for review authors: Working on a protocol or review? Here are a few important things to bear in mind:

- Don’t leave the protocol or review ‘checked out’ when you’re not working on it. Check it back into Archie after every session.
- Extracted data but not sure how to present it? Talk to the Managing Editor before entering data to RevMan.
- If you are planning to use GIV data, please get in touch when you enter the data – we have found it can go badly wrong and it’s better to get the data entered correctly from the outset than have to rewrite the review during the editorial process.
- In your review, follow the methods you had set out in your protocol. If there’s a good reason for taking a different course, make this plain in the review.
- Be prepared for multiple iterations of your protocol or review after the first submission. Work is rarely accepted for publication immediately after it has been resubmitted following editorial or peer review.
- Make sure that everyone on your team has activated their Archie accounts otherwise the publication process can be severely delayed.

Information management news from Liz Stovold

The new Cochrane Register of Studies (CRS) is finally here!! I’ve been busy transferring the CAG register of trials across to the new platform. The CRS offers opportunities to share and handle references more simply, link multiple references to studies, and link studies to reviews. This project is still in the early stages, and the full functionality of the CRS is not yet up and running, but this is a great step forward in reducing duplication of effort in organising references and studies. Please bear with us if you are waiting for a literature search as the search strategies for each review need to be migrated to the new software.
Review Group Activities 2012

The Group’s main task is to coordinate the preparation and publication of systematic reviews. Details of our recent work in this area are given below. Completed reviews and protocols are published on The Cochrane Library which can be accessed at www.thecochranelibrary.com

Reviews Published, The Cochrane Library, 2012

Airway clearance techniques for COPD (Osadnik CR, McDonald CF, Jones AP, Holland AE)

Chronic obstructive pulmonary disease (COPD) is an umbrella term for chronic lung conditions characterised by airflow obstruction that cannot be fully reversed, such as emphysema and chronic bronchitis. Individuals with COPD often experience breathlessness, cough and sputum which may worsen during acute flare-ups. Airway clearance techniques (ACTs) are techniques that aim to clear sputum from the lungs. The usefulness of ACTs for individuals with acute flare-ups of COPD or stable COPD has been difficult to ascertain.

This review comprised 28 studies of 907 participants, with the quality of evidence being generally poor. Performing ACTs during an acute flare-up of COPD reduced the likelihood of needing mechanical assistance to breathe, as well as the length of time for which it was required. Time spent in hospital was slightly reduced, but there was little evidence to suggest any benefit on future flare-ups or health-related quality of life.

Performing ACTs during stable COPD did not appear to affect flare-ups or hospitalisations, however it may improve health-related quality of life.

Techniques which involve breathing out against a positive expiratory pressure resistance may provide greater benefits than other types of ACTs. The lack of adverse events observed in this review suggests that ACTs are safe for individuals with COPD.


Asthma is a condition that affects the airways (tubes carrying air in and out of the lungs). During an asthma exacerbation (attack), the airways narrow and drugs can be taken to dilate, or widen, the airways. Common bronchodilators (medicines used to widen the airways) are short-acting beta2-agonists (e.g. salbutamol) or anticholinergics (e.g. ipratropium bromide). In this review, we examined if the use of anticholinergic inhalers during an asthma attack in children aged over two years is effective compared to either placebo or another bronchodilator. We also looked at combinations of anticholinergic plus a beta2-agonist compared to an anticholinergic on its own.

We found six small trials of unclear quality answering these two questions. We found data from four trials on 171 children comparing anticholinergics with beta2-agonists. Children on anticholinergics alone were significantly more likely to experience treatment failure than those on beta2-agonists (odds ratio (OR) 2.27; 95% CI 1.08 to 4.75). We also found data from four trials on 173 children comparing children on anticholinergics alone with children on anticholinergics plus beta2-agonists. In this case,
treatment failure was more likely in children taking anticholinergics only than if they were combined with beta2-agonists (OR 2.65; 95% CI 1.2 to 5.88). We were only able to combine data for treatment failure and hospitalisation.

In summary, we found that inhaled anticholinergics used on their own are less effective than inhaled beta2-agonists used alone or in combination with anticholinergics. Inhaled anticholinergics seem safe, with no significant side effects apparent.

**Leukotriene receptor antagonists in addition to usual care for acute asthma in adults and children (Watts K, Chavasse RJPG)**

Current recommended treatment in the emergency department for people experiencing an asthma attack is beta2-agonists, systemic corticosteroids and oxygen. Unfortunately, some people do not get better with these standard treatments and so there is interest in developing additional treatments which will help people experiencing an asthma attack. One such treatment is antileukotrienes, which are available in tablet form to be taken orally; this drug is also made in injection form, however the intravenous form is not marketed and therefore not available.

This review considers the effect of antileukotriene agents, (normally used as add-on preventer therapy in chronic asthma), when used during acute asthma treated in emergency settings. We identified eight randomised controlled trials (RCTs) on 1470 adults and 470 children addressing this question, and in most of these studies participants were also given courses of corticosteroids at the time of treatment. We did not find a significant difference in the likelihood of being admitted to hospital between people treated with oral antileukotrienes and placebo or usual care. There was no significant difference in participants requiring additional care (including hospital admission or other treatment options) at the end of the studies between treatment and control groups. There was an improvement in lung function in people taking antileukotrienes compared to those on placebo. More research in this area is required, and the low number of studies recruiting children does not enable us to provide evidence on what effects this class of drugs has in children.

There were two trials that randomised 772 adults and 276 children to receive intravenous antileukotrienes and there was no statistically significant difference in hospital admissions, however there was an improvement in lung function in adults on antileukotrienes.

**Long-acting beta2-agonist in addition to tiotropium versus either tiotropium or long-acting beta2-agonist alone for COPD (Karner C, Cates CJ)**

Chronic obstructive pulmonary disease (COPD) is a lung disease which includes the conditions chronic bronchitis and emphysema. The symptoms include breathlessness and a chronic cough. COPD is an irreversible disease that is usually brought on by airway irritants, such as smoking or inhaled dust.

Long-acting beta2-agonists and tiotropium are two types of inhaled medications that help widen the airways (bronchodilators) for up to 12 to 24 hours. These bronchodilators are commonly used to manage persistent symptoms of COPD. They can be used in combination or on their own. These bronchodilators work in different ways and therefore might be more beneficial if used together. The purpose of this review was to determine the benefits and risks of using a combination of both types of bronchodilator compared to the individual bronchodilators.

We found five studies involving 3263 patients comparing the long-term efficacy and side effects of combining tiotropium with a long-acting beta2-
agonist. The combination of tiotropium plus long-acting beta2-agonist resulted, on average, in a slightly better quality of life and lung function for the patients compared to using only tiotropium, but did not show a difference in hospital admissions or mortality. There were not enough data to determine the risks and benefits of tiotropium plus long-acting beta2-agonist treatment compared to long-acting beta2-agonist alone.

**MSG avoidance for chronic asthma in adults and children (Zhou Y, Yang M, Dong BR)**

Monosodium glutamate (MSG) is used as a flavour enhancer and has been implicated in "Chinese Restaurant Syndrome", causing tightness, burning or numbness in the face, neck and upper chest (although there is no evidence to prove this syndrome). It has also been proposed that asthmatics may react badly to MSG. In two randomised controlled trials (RCTs), involving 24 adult asthmatics, there was no evidence that MSG worsened asthma when compared to control ingestion. Further RCTs are needed.

**Tiotropium versus placebo for COPD (Karner C, Chong J, Poole P)**

Chronic obstructive pulmonary disease (COPD) is a lung disease which includes the conditions, chronic bronchitis and emphysema. It is caused by smoking or inhaled dust, which leads to blockage or narrowing of the airways. The symptoms include breathlessness and a chronic cough. Tiotropium is an inhaled medication that helps widen the airways (bronchodilator) for up to 24 hours, and is used to manage persistent symptoms of COPD.

We found 22 studies including 23,309 participants, comparing the long-term effectiveness and side effects of tiotropium and placebo. Compared with placebo, tiotropium treatment led to an improvement in quality of life, fewer people had an exacerbation (worsening of COPD symptoms), or exacerbations leading to hospital admissions. The number of people that needed to be treated for a year, for one person to avoid one additional exacerbation was 16 (95% confidence interval (CI) 10 to 36). We found no statistically significant difference between the tiotropium and placebo groups in terms of the number of hospital admissions for any cause, serious adverse events or deaths during the studies. However, when we divided the data depending on whether a dry powder inhaler or a soft mist inhaler was used in the studies, these two subgroups were significantly different. With the dry powder inhaler there were fewer deaths in the tiotropium group than in the placebo group, whereas with the soft mist inhaler there were significantly more deaths in the tiotropium group than in the placebo group. Also, there was a larger number of participants that stopped study medication early in the placebo group than in the tiotropium group.

This review shows that treatment with tiotropium improves patients' quality of life, and reduces the risk of exacerbations, including exacerbations leading to hospitalisation. But tiotropium does not reduce hospitalisations for all causes or the number of deaths. Based on the evidence in this review, tiotropium appears to be a reasonable treatment choice for patients with stable COPD. However, the review also shows that tiotropium delivered via the Respimat soft mist inhaler is associated with an increased risk of death, which calls for both caution and further investigation.
Protocols Published

**The Cochrane library, 2011**

- Addition of anti-leukotriene agents to inhaled corticosteroids in children with persistent asthma (Chauhan BF, Ben Salah R, Ducharme FM)
- Antibiotics for persistent cough or wheeze following acute bronchiolitis in children (McCallum GB, Morris PS, Chang AB)
- Beclometasone for COPD (De Coster DA, Jones M)
- Bronchial thermoplasty for moderate or severe persistent asthma in adults (Yepes-Nuñez JJ, Torrego A, Solà I, Alonso-Coello P, Plaza V, Roqué i Figuls M)
- Different systemic corticosteroid regimens for the emergency management of acute asthma (Johnson K, Stang AS, Johnson DW, Rowe BH, Hartling L)
- Helminths for asthma (Croft AM, Bager P, Kumar S, Manning P)
- Inhaled corticosteroids in children with persistent asthma: dose-response effects on growth (Zhang L, Prietsch SOM, Ducharme FM)
- Intermittent versus daily inhaled corticosteroids for persistent asthma in children and adults (Chauhan BF, Chartrand C, Ducharme FM)
- Mycophenolate mofetil (MMF) for the treatment of connective tissue disease-associated interstitial lung disease (ILD) (Stolagiewicz NE, Draper A, Schomberg LEE, Chua F)
- Overview of the safety of regular formoterol or salmeterol in children with asthma (Cates CJ, Stovold E)
- Prophylactic antibiotic therapy for chronic bronchitis and chronic obstructive pulmonary disease (COPD) (Poole P, Herath SC)
- Swimming training for asthma in children and adolescents aged 18 years and under (Beggs S, Foong YC, Le HCT, Mohammed Noor WD, Walters JAE, Wood-Baker R)
- Tai Chi for chronic obstructive pulmonary disease (COPD) (Ngai SPC, Jones AY, Tam W)
- Tiotropium versus ipratropium bromide for chronic obstructive pulmonary disease (Cheyne L, Irvin-Sellers MJ, White J)