**Managing Chronic Wet Cough in Children: Another piece of the puzzle**

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Chronic wet cough is the hallmark of COPD in the elderly and bronchiectasis in adults and older children. In young children, the commonest cause of chronic wet cough is protracted bacterial bronchitis (PBB) but there are large gaps in our understanding of this high prevalence condition.1 This includes the optimal treatment strategy to control symptoms, prevent recurrence, and reduce long-term morbidity. Such issues highlight the inequalities experienced by children with respiratory disease compared to affected adults. Addressing this imbalance to improve children’s respiratory health is vital, as we know early life factors such as respiratory infections are associated with reduced lung function that tracks with the child through adolescence and into adulthood.2

PBB is a chronic endobronchial infection causing a persistent, troublesome cough that adversely affects the child’s quality of life and that of their family. Informed by the common causative organisms,3 first-line treatment is oral amoxicillin / clavulanic acid (co-amoxiclav) but the optimum duration is unknown. International guidelines recommend between two4,5 and six6 weeks resulting in a variety of clinical practice.1 Relapses of PBB occur in up to three quarters of cases and recurrent PBB (>3 episodes per year) is associated with future bronchiectasis.7 However, we do not know what causes relapses or how they should be treated. In The Lancet Respiratory Medicine, Tom Ruffles and colleagues have started to address the first of these issues with a randomised, placebo controlled trial of antibiotic duration in children with suspected PBB.8

In the article, one hundred and six Australian children with a median age of two years, presenting with chronic wet cough and suspected of having PBB were randomised to receive two weeks co-amoxiclav (plus two weeks placebo) or four weeks co-amoxiclav. The primary outcome was cough resolution by day 28. Participants were followed-up for six months and secondary outcomes included time till next exacerbation, PBB relapse, quality of life and antimicrobial resistance.

By four weeks, cough resolution was achieved in two-thirds and parents reported improved quality of life. However, these outcomes were not significantly different between the groups (adjusted relative risk for cough resolution (95% CI) 0.87 (0.60, 1.28), p=0.49) with slightly fewer children who received a four-week course of co-amoxiclav achieving this (61.5% versus 70.4%). The trend for lower cough resolution in the four-week group may be explained by baseline differences in cough duration and previous antibiotic use between groups.

This trial provides important evidence for the treatment of children with chronic wet cough and may enable us to refine the broad PBB diagnostic criteria. It confirms children with suspected-PBB are a heterogeneous group. One third of Australian children with a clinical suspicion of PBB did not subsequently meet the diagnostic criteria due to failure to achieve cough resolution. Although two-week data is not presented, the lack of difference in cough resolution between groups, suggests for non-responders there is little apparent benefit in extending the antibiotic course beyond two weeks as currently recommended.4,5 These children should instead be investigated for a cause other than PBB.

However, the story appears somewhat different for children who do improve following initial treatment. In the 70 children who achieved cough resolution by 28 days, and therefore had a confirmed diagnosis of PBB, the median time to next wet cough exacerbation was longer in the four-week than the two-week group (150 vs 35.5 days, p=0.02). There was also a trend for a lower rate of PBB relapse in the four-week group (53.1% vs 73.7%, p=0.07). As relapses are common and recurrent PBB is associated with longer-term morbidity, these differences may be important enough to warrant a longer initial course in responders. Making such a recommendation based on this study is difficult as the six-month follow-up does not allow assessment of recurrent-PBB which is the outcome associated with future bronchiectasis.

Advocates of a prolonged initial antibiotic course in PBB have long argued that extending the initial treatment beyond that required for symptom resolution, enables damaged epithelium to repair and mucociliary clearance to improve, thereby reducing relapses.6 This is supported by a recent retrospective review which found an inverse association between the duration of initial antibiotic course and subsequent rates of recurrent PBB.9 This raises the possibility that children with PBB may benefit from an initial six-week antibiotic course to reduce relapses, antibiotic burden and potentially bronchiectasis. This must be balanced against the risk that inappropriate antibiotic use will promote antimicrobial resistance. A further RCT in children with PBB, assessing two versus six weeks antibiotics using carefully chosen outcomes10 and follow-up of at least 12 months may provide the final piece of the puzzle. Such an RCT along with other well-designed studies in children with respiratory disease are vital to optimise children’s respiratory health and improve the future respiratory health of the whole population.

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