3-Day or 5-Day Oral Antibiotics for Non-severe Pneumonia in Children?

Haider BA, Saeed MA, Bhutta ZA. Short-course versus long-course antibiotic therapy for non-severe community-acquired pneumonia in children aged 2 months to 59 months. Cochrane Database of Systematic Reviews 2008; 2: CD005976. This version first published online: 16 April 2008.

INTRODUCTION

Treatment of pneumonia requires an effective antibiotic used in adequate doses for an appropriate duration. Recommended duration of treatment ranges between 5 and 14 days depending on the etiology and severity of pneumonia. Shorter duration of therapy could be particularly important in resource poor settings with poor access to health care, and limited budget. The present review was aimed at evaluating the efficacy of 3d *vs*. 5d therapy with the same antibiotic for non-severe community-acquired pneumonia in children between 2 to 59 months.

SUMMARY

Three randomized controlled trials (RCTs) enrolling a total of 5,763 children aged 2 to 59 months were included. Two multicentric trials (one each from India and Pakistan) compared 3 days versus 5 days of oral amoxicillin whereas one trial conducted in Indonesia and Bangladesh used cotrimoxazole for same comparison. The World Health Organization (WHO) definitions were used for diagnosis of pneumonia as well as for clinical cure and treatment failure. Analysis of three days versus five days of treatment with the same antibiotic for non-severe pneumonia in children showed non-significant differences in rates of clinical cure at the end of treatment (RR 0.99; 95% CI 0.97 to 1.01), treatment failure at the end of treatment (RR 1.07; 95% CI 0.92 to 1.25) and relapse rate after seven days of clinical cure (RR 1.09; 95% CI 0.83 to 1.42). Subgroup analysis undertaken on the basis of whether amoxicillin or cotrimoxazole was used also showed non-significant differences for these outcomes between 3 days and 5 days of therapy. Outcomes of mortality at one month and additional interventions used could not be evaluated in this review due to non-availability of data from the included studies. The authors concluded that a short course (three days) of antibiotic therapy is as effective as a longer treatment (five days) for non-severe pneumonia in children under 5 years of age.

COMMENTARY

Are the results valid?

The problem addressed in this review is specific and relevant. The search of literature was as per criteria laid down by the Cochrane group. All the included studies were large and multicentric, each enrolling nearly 1,000 children in each arm. All had rigorous methodology though in one study, allocation concealment and follow-up loss was uncertain because of it being unpublished yet. The blinding between the additional drug dosages and placebo was done in these studies but the conclusions would have been sounder if the outcome assessors would not have known whether they are assessing the respiratory rate before or after therapy. There was no significant heterogeneity among the trials for the outcomes assessed.

The outcomes such as clinical cure rate, treatment failure and relapse rate were functionally important but the diagnosis of pneumonia was based solely on the assessment of respiratory rate cut-offs as defined by the WHO. Also, the disappearance of fever and the patient well being were not taken into account for defining clinical cure. The limitations of respiratory rate based diagnosis of pneumonia are well known and include overdiagnosis because of inclusion of cases of asthma and other respiratory ailments(1). Thus these results are valid only for the cases of pneumonia diagnosed purely on the basis of counting respiratory rate.

COCHRANE CONCLUSION

- A short course (3 days) of oral antibiotic therapy is as effective as a longer treatment (5 days) for non-severe pneumonia in children under five years of age.

OUR CONCLUSION

- These results are valid only for cases of pneumonia diagnosed on the basis of fast breathing as defined by age specific cut-offs and performance is likely to be different in true cases of bacterial or radiological pneumonias.

Clinical importance and Precision of the Results

Shortening the duration of antibiotic therapy in pneumonia is likely to improve compliance and decrease the cost of therapy. However, incomplete eradication of the organism because of shorter duration of therapy carries the potential risk of development of resistant organisms. Although two of the included studies tried to assess the colonization with pathogenic bacteria with two durations of therapy, this outcome has not been evaluated in this review.

It is likely that a large chunk of included cases could be of viral etiology where anyway the duration of antibiotics is not going to matter. Therefore, the actual sample size of cases of true bacterial pneumonia would be much less in included studies. Some recent studies have shown that only a very small proportion of children diagnosed with pneumonia by the WHO criteria had radiological evidence of pneumonia(2). The possibility that a large proportion of cases included in the study were not actually cases of bacterial pneumonia is further supported by the fact that 90% of the patients responded to the treatment in either arm of the studies. It would have been interesting to know the true quantum of benefit by including another arm of only placebo for 5 days and noting the proportion of patients which would have actually improved even without any antibiotic therapy. However, such a study would have ethical concerns as antibiotic treatment has been recommended as a standard therapy by the WHO on the basis of the respiratory rate cut-offs. The competing interests also can not be ruled out as at least two of the three studies were sponsored or funded by the WHO.

Implications for Practice and Policy

Present WHO and IMCI guidelines recommend 5 day antibiotic therapy for pneumonia. Shorter course of antibiotic therapy may be recommended in future by WHO for treatment of pneumonia in developing countries. However, it is to be noted that these results are valid only for cases of pneumonia diagnosed on the basis of fast breathing as defined by age specific cut-offs. For individual pediatrician's practice where the diagnosis of pneumonia is based on a combination of respiratory distress, auscultatory and radiological findings, the duration of treatment also would continue to be guided by the clinical response which would include disappearance of fever and toxemia along with normalization of respiratory findings.

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