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From the authors:

We would like to thank M. Korppi for his comments regarding our recently published study on the use of clarithromycin in the treatment of respiratory syncytial virus (RSV) bronchiolitis [1].

RSV is the most common cause of upper and subsequent lower respiratory tract infection in children and it is most severe in children aged 8–30 weeks [2]. Despite many attempts to find effective treatments for patients with RSV bronchiolitis, no consistently effective therapy has yet been described. Since RSV infection initiates an immune inflammatory response that may produce long-lasting harmful effects, in our study we hypothesised that we could modify the course of the disease and prevent wheezing after bronchiolitis by administering macrolides (due to their anti-inflammatory effect) to infants during an acute episode of RSV bronchiolitis. Despite the small number of children in each group, the results of the study were exciting for us. This is important, as, to date, there has been no effective therapy for RSV bronchiolitis. Our results should encourage the undertaking of further studies to confirm the use of clarithromycin in RSV bronchiolitis, especially in infants aged <6 months who present with severe disease.

In our study, *Bordetella pertusis* was not investigated since all subjects tested positive for RSV and presented normal leukocyte counts, with leukocytosis (15,000–100,000 cells·mm^{-3}) being characteristic of *B. pertusis* infection [3].

We did not investigate *Simcania negevensis* or *Chlamydia trachomatis*. Although in some populations the involvement of *S. negevensis* seemed to be common in association with RSV bronchiolitis [4, 5], results of one study [6] did not reveal any significant difference in the prevalence of *S. negevensis* infection between children with bronchiolitis and control subjects. In that study of 188 patients and 110 healthy control subjects, *S. negevensis* serological assays were positive in 18% of patients compared with 29% of control subjects [6].

We did not investigate *C. trachomatis* but we know that pneumonia due to *C. trachomatis* develops in 10–20% of infants born to females with chlamydial infection. *C. trachomatis* pneumonia of infancy has a very characteristic presentation and auscultation reveals rales while wheezing is uncommon. A distinctive laboratory finding is the presence of peripheral eosinophilia (>400 cells·mm^{-3}) [7]. In our study group, only one child had eosinophilia.

The use of bronchodilator agents continues to be controversial. The results of the meta-analysis indicated that some children treated with bronchodilators might have a transient improvement in clinical score [8]. Although there is no evidence from randomised controlled trials to justify the routine use of bronchodilators, clinical experience suggests that, in selected infants, there is an improvement in the clinical condition after bronchodilator administration [9–12]. In our study, the infants received β_2-agonist treatment based on clinical parameters, including the presence of wheezing on auscultation of the chest or respiratory distress with retractions. Wheeze and chest tightness has traditionally been associated with enhanced bronchial responsiveness. Airway hyperresponsiveness appears to be one manifestation of the airway inflammation induced by RSV. It has been shown that a correlation exists between airway inflammation and the degree of airway hyperresponsiveness (as discussed in our paper). Following this, duration of the need for β_2-agonist treatment (even for minimal improvement in clinical condition) may provide some indication as to the degree of airway inflammation.

In the process of re-analysis of the data for readmission, we realised that there was a data entry error. Unfortunately, this changes the statistical significance in the readmission rate. In our study, five patients were readmitted to hospital with wheezing within 6 months of discharge: four (44%) from the placebo group and one (8.3%) from the clarithromycin group. Although the values were higher in the placebo group, this difference did not reach significance, which may be attributed to the small number of children in each group.

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STATEMENT OF INTEREST

None declared.

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Antibiotics in RSV bronchiolitis: still no evidence of effect

To the Editors:

Avoiding unjustified antibiotic use is of paramount importance in order to decrease worldwide development of resistance. In this context, the study by TAHAN *et al*. [1], which reports the results of a randomised, double-blind, placebo-controlled trial comparing clarithromycin 15 $mg \cdot kg^{-1} \cdot day^{-1}$ for 3 weeks with placebo in infants with respiratory syncytial virus (RSV) bronchiolitis, is disturbing. Careful analysis of the study shows important methodological flaws, making the results unreliable and the recommendations premature.

First, the trial has not been registered at www.controlled-trials.com, which is now a prerequisite for randomised controlled trials (RCTs) [2]. Secondly, and even more importantly, the RCT lacks a proper power analysis. In the design of an RCT it is necessary to know beforehand how large a sample is needed to enable statistical judgments that are accurate and reliable. The sample size seems to be too small to draw any evidence-based conclusions. Moreover, it is not known if patients with prior use of antibiotics were excluded from the analysis. Finally, why did TAHAN *et al*. [1] choose to use an antimicrobial drug that must be administered for 3 weeks, while the length of stay in the control group is only 88 h?

Numerous studies have shown that the occurrence of a secondary or concurrent bacterial infection in hospitalised children with RSV lower respiratory tract disease (LRTD) is <1% [3]. Despite this, nearly half of all hospitalised infants with RSV LRTD are treated with antibiotics [4–6]. This unjustified use of antibiotics must be avoided, because of the close link with the development of antimicrobial resistance [7]. Therefore, there is a rationale for a properly designed RCT equivalence trial studying antibiotics in hospitalised infants with RSV LRTD.

Unfortunately, studies such as the one by TAHAN *et al.* [1] do not provide a justified basis for the treatment of hospitalised infants with respiratory syncytial virus and do not help in a reduction of abuse of antibiotics.

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STATEMENT OF INTEREST

None declared.

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