

Correspondence

Further clinical trials on macrolides for bronchiolitis in infants are unnecessary

To the Editor:

We read with interest results of the randomized controlled trial (RCT) conducted by Beigelman et al¹ involving 40 hospitalized infants with respiratory syncytial virus (RSV) bronchiolitis. They report that compared with placebo, a 2-week course of once-daily azithromycin reduced IL-8 levels in nasal lavage fluid, but not in serum. Although no significant between-group differences were observed in the proportions of infants experiencing 2 or more parent-reported wheezing episodes in the subsequent 50 weeks, there was some evidence that those treated with azithromycin took longer to have a third episode of wheezing and they had fewer days with respiratory symptoms during follow-up. In light of these findings, the authors called for larger clinical trials to evaluate azithromycin for recurrent wheezing after RSV hospitalization for bronchiolitis. However, we wish to highlight that 5 RCTs have already been published evaluating different doses and durations of macrolides for those hospitalized with bronchiolitis.²⁻⁶ Nonetheless, just 1 small RCT comprising 30 infants² was cited as the “only previous trial for the prevention of post-RSV wheezing.”¹ This Turkish study reported clinically improved outcomes during hospitalization and contrasts with the other 4 trials (range, 71-219 subjects) in which no clinical benefits were detected in infants from The Netherlands, Brazil, Australia, and New Zealand.³⁻⁶

However, only 3 of the 5 published RCTs reported clinical data beyond the hospitalization period.^{2,5,6} The Turkish study suffered an attrition rate of 30%, leaving only 21 infants to be followed for the next 6 months, with 1 of the 12 infants allocated 3 weeks of daily clarithromycin and 4 of the 9 treated with placebo requiring a respiratory illness readmission, a result that did not reach statistical significance.² The other 2 studies from Australia and New Zealand involved a combined total of 316 infants (89% Indigenous infants, 44% RSV) who received single large once-weekly doses of azithromycin on either 1 or 3 occasions, doses that were equivalent to 7-day⁶ or 3-week⁵ treatment, respectively. In each of these studies, participants were followed for 6-months post-hospitalization. In both studies, we found that despite azithromycin significantly reducing nasopharyngeal bacterial carriage, it did not improve short-term clinical outcomes (length of hospitalization, duration of oxygen supplementation) or respiratory readmissions within 6-months of hospital discharge. Between-group differences at the day-21 clinical review were also not significant, and persistent wheezing was reported in 11% of the infants in the azithromycin group compared with 10% of the infants in the placebo group.⁵ With respect to respiratory readmissions, data from both studies revealed that 101 infants were readmitted (azithromycin 57, placebo 44), of whom

70% were admitted for wheezing episodes.^{5,6} Thus, azithromycin did not provide immediate or longer-term (6-months) clinical benefits in bronchiolitis for infants regarded as being at high risk of disease severity and readmission for respiratory illnesses.⁷

Although the dose and regime in the study by Beigelman et al are different, we believe that these previously published 5 RCTs demonstrate that there is no evidence of macrolides being beneficial for infants with bronchiolitis and further clinical trials are unnecessary. Moreover, reduced use of azithromycin will improve antimicrobial stewardship, decrease potential adverse events, and reduce costs.

Gabrielle B. McCallum, BNursing, MPH, PhD^a

Anne B. Chang, MBBS, FRACP, PhD^{a,b}

Keith Grimwood, MB, ChB, FRACP, MD^c

From ^aMenzies School of Health Research, Charles Darwin University, Casuarina, Australia; ^bQueensland Children's Medical Research Institute, Children's Health Queensland, Queensland University of Technology, Brisbane, Australia; and ^cGriffith University and Gold Coast University Hospital, Southport, Australia E-mail: gabrielle.mccallum@menzies.edu.au.

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