Antibiotics for bronchiolitis in children


Background
Bronchiolitis is a serious, potentially life-threatening respiratory illness commonly affecting babies. It is often caused by respiratory syncytial virus (RSV). Antibiotics are not recommended for bronchiolitis unless there is concern about complications such as secondary bacterial pneumonia or respiratory failure. Nevertheless, they are often used by clinicians.

Objectives and Methods
The authors conducted a systematic review to study the evidence for the usefulness of antibiotics in treating bronchiolitis compared to placebo or other interventions. They searched the Cochrane Central Register of Controlled Trials which includes the Cochrane Acute Respiratory Infection Group’s Specialised Register, and the Database of Abstracts of Reviews of Effects, MEDLINE, EMBASE and Current Contents.

They included seven randomised controlled trials (RCTs) comparing antibiotics to placebo in children under two years diagnosed with bronchiolitis (total of 824 participants). Two of these studies also compared intravenous and oral antibiotics.

The primary outcome was duration of symptoms/signs (duration of supplementary oxygen requirement, oxygen saturation, wheeze, crepitations (crackles), fever). Secondary outcomes included duration of admissions/time to discharge from hospital, readmissions, complications/adverse events (including death) and radiological (X-ray) findings. They included two new studies (281 participants), both comparing azithromycin with placebo.

Results
They found no significant difference for length of hospital stay, duration of oxygen requirement and readmission. These results were similar to an older study (52 participants) that demonstrated no significant difference comparing ampicillin and placebo for length of illness.

One small study (21 participants) with higher risk of bias randomised children with proven RSV infection to clarithromycin or placebo found a trend towards a reduction in hospital readmission with clarithromycin.

The three studies providing adequate data for days of supplementary oxygen showed no difference between antibiotics and placebo (95% confidence interval (CI) -0.72 to 0.33). The three studies providing adequate data for length of hospital stay similarly showed no difference between antibiotics (azithromycin) and placebo (95% CI -1.18 to 0.02).

Two studies randomised children to intravenous ampicillin, oral erythromycin and control and found no difference for most symptom measures.

There were no deaths reported in any of the seven included studies. No other adverse effects were reported.

The authors conclude:
There is no evidence to support the use of antibiotics for bronchiolitis, although research may be justified to identify a subgroup of patients who may benefit from antibiotics.

Discussion:
The main concern among clinicians is that if they do not use antibiotics in a child presenting with a fever and clinical symptoms and signs of bronchiolitis, they may be putting the child at risk of serious complications such as pneumonia, sepsis and death. Studies have shown that that children with this presentation are very unlikely to have an occult bacteraemia. The clinical scenarios associated with a higher risk of bacterial co-infection include 1) children...
with a serious illness requiring admission to intensive care, and especially those requiring ventilation, 2) nosocomial respiratory syncytial virus (RSV) infection (6.5% bacteraemia),
3) cyanotic congenital heart disease (6.6% bacteraemia) and 4) bronchiolitis and respiratory failure (20% bacterial pneumonia). In these situations, use of antibiotics may be justified.

Expert Comments from CMC faculty - Dr. Sneha Titus, Professor, Department of Child Health

I strongly agree with the argument that the use of antibiotics in bronchiolitis should be limited and antibiotics should be given for those who have risk factors (identified in various studies) as discussed above.

The title of this review implies that it will answer the question “Is it safe to treat an infant with bronchiolitis without antibiotics” as there is a concern about secondary bacterial infection in some cases. The author’s search strategy identified 7 studies in which antibiotic vs. placebo was used in the treatment of bronchiolitis. But in 3 out of 7 studies, the investigators had used macrolide antibiotic more for its anti-inflammatory or immunomodulatory effect than for its anti bacterial effect. Hence concurrent use of other antibiotics was allowed during the course of study. Mc Callum et al reported that 70-72% of subjects received antibiotics and Pinto et al reported antibiotic use in 4.5-6.3% of the subjects. In the third study in which only RSV positive infants were included, use of antibiotics was not an exclusion criteria but there is no mention of how many patients were on other antibiotics (Tahan et al).

A fourth study (Kneyber et al) included in the review, did not allow use of other antibiotics while azithromycin/placebo was being given. It is interesting that in that study 64% of the patients (parents) approached, did not consent for the study and likely that the patients the investigators eventually recruited had bronchiolitis of milder severity. (mean symptom score of 3.5 to 4.5 where maximum score is 12)

There are 3 other studies included where the objective of the study was to look for difference in outcome when bronchiolitis patients were treated with or without antibiotics. Two studies from Bangladesh (Kabir et al, Mazumdar et al) which the review authors considered as methodologically inferior (not blinded) and a 1966 study from UK (Field et al) used antibiotic ampicillin/azithro vs. placebo and showed there was no significant difference between the groups.

Hence I feel the conclusion of the authors of this review that “There is no evidence to support the use of antibiotics for bronchiolitis” may be misleading as many of the studies included were not designed to investigate the role of antibiotics for its antibacterial effect but to look at the benefit of macrolides in bronchiolitis.

More studies specifically designed to see if outcome differs when antibiotics are given or withheld are needed. Meanwhile in day to day paediatric practice, categorising patients according to risk and using standard protocol for inpatient management wherein antibiotics are avoided / limited in the low risk group, will bring down unnecessary antibiotic use.