Study: Children with pneumonia leaving hospital can have antibiotic treatment reduced to three days

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The results of the largest study in a high-income country looking at antibiotic dosing and duration for children hospitalized with pneumonia

show that the number of doses given can be reduced safely, without impacting recovery.

Pneumonia (sometimes called a chest infection) is common in young children. It is usually treated with the antibiotic amoxicillin. But, until now, there has been little evidence to guide how long treatment should be given for, or what dose should be used.

The study, funded by the National Institute for Health Research (NIHR), published today in the *Journal of the American Medical Association* (*JAMA*), found children only required three days of amoxicillin (given by mouth) rather than the five or seven days more commonly given internationally. Led by researchers at St George's, University of London and the MRC Clinical Trials Unit at UCL, the CAP-IT trial results will likely influence national and international guidelines for treating children who attend hospital with pneumonia, reducing the treatment burden for children and their caregivers.

The randomized controlled clinical trial recruited 824 children (of whom 814 received at least 1 dose of trial medication), aged greater than six months and weighing 6 to 24 kg from 29 hospitals in the UK and Ireland. The study was double-blind and placebo-controlled, with half the participants receiving seven days of amoxicillin and the other half receiving three days of amoxicillin and four days of placebo. As well as comparing duration, dosing was also studied, with half the participants in each duration group receiving a lower dose (35 to 50 mg/kg) and the other half a higher dose (70 to 90 mg/kg).

The results found that the shorter course of treatment was no less effective than the longer course, and that the lower dose was no less effective than a higher dose, in terms of children needing further antibiotic treatment within four weeks. The study also used a dosing schedule of only giving amoxicillin in two doses per day, rather than

three, suggesting the total number of doses required to treat pneumonia could be reduced from 15 to 21 doses over five to seven days (UK guidelines currently recommend three times daily dosing for five days) to the simpler six doses over three days.

The trial found no differences in symptoms between the different durations or doses given, other than resolution of cough being slightly quicker in the group receiving seven days of amoxicillin (10 days recovery vs. 12 days). There was no difference in time to return to normal activities for parents and children, or in additional use of healthcare services. The number of adverse events, such as diarrhea, thrush and skin rash, was also comparable between groups. There was no evidence that using shorter course or lower dose amoxicillin led to increased resistance to the pneumococcus bacteria, the leading bacterial cause of pneumonia globally, with low resistance levels overall in the UK.

Dr. Julia Bielicki, joint first author on the paper from St George's, University of London, said: "Amoxicillin is the commonest antibiotic children receive globally, with hundreds of millions of courses given every year. There is surprisingly limited evidence of the optimal dose and duration that should be used to make sure children are treated safely, minimizing the impact from side effects and antibiotic resistance, while making it simpler for families to give their child the medicines they need.

"The CAP-IT study provides family-friendly evidence that shorter durations of amoxicillin given twice daily are safe and effective even in young children with serious chest infections attending hospital. It has also demonstrated again that large strategic trials that inform the optimal choice of drug, dose and duration of antibiotics to treat common infections are feasible and critical to tackling antibiotic resistance."

Professor Diana Gibb, joint last author on the paper from the Medical Research Council Clinical Trials Unit at UCL, London said: "CAP-IT is one of the largest antibiotic trials involving children globally, and clearly shows that for children leaving hospital with a diagnosis of pneumonia, three days of amoxicillin is safe and effective. We are immensely grateful to all the children and their families who joined the trial; for the work done by nurses and doctors at the participating hospitals, and to the PERUKI and GAPRUKI networks who helped make the trial a success."

UK Special Envoy on Antimicrobial Resistance Dame Sally Davies, said: "I welcome the CAP-IT trial results for adding to the increasing evidence on optimal prescribing. Thanks to the UK National Institute of Health Research, CAP-IT gives information that can be used in the real world by families, doctors and policy-makers to improve health outcomes, whilst contributing to global stewardship efforts. We need many more studies in adults and children globally to ensure that we can continue to tackle the global challenge of AMR."

Dr. William van't Hoff, chief executive officer at the NIHR Clinical Research Network Coordinating Centre, said: "Each year, nearly half of all children under two years receive antibiotics, commonly for acute respiratory infections. I am delighted to see that the CAP-IT study has provided key evidence on the best use of antibiotics for community-acquired pneumonia which is really important to improving care for so many children. It's a trial that has been supported across the UK and in Eire, demonstrating the power of collaborative research in tackling major health questions."

More information: Julia A. Bielicki et al, Effect of Amoxicillin Dose and Treatment Duration on the Need for Antibiotic Re-treatment in Children With Community-Acquired Pneumonia, *JAMA* (2021). DOI: 10.1001/jama.2021.17843

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