The early use of Antibiotics for at Risk CHildren with InfluEnza-like illness (ARCHIE): a double-blind randomised placebo-controlled trial

Kay Wang[1], Malcolm G. Semple[2,3], Michael Moore[4], Alastair D. Hay[5], Sharon Tonner[1], Ushma Galal[1], Jenna Grabey[1], Tricia Carver[1], Rafael Perera[1], Ly-Mee Yu[1], Jill Mollison[1], Paul Little[3], Andrew Farmer[1], Christopher C. Butler[1] and Anthony Harnden[1]

[1]Nuffield Department of Primary Care Health Sciences, University of Oxford, Radcliffe Primary Care, Oxford, UK. [2]NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, Institute of Infection, Veterinary and Ecological Sciences, University of Liverpool, Liverpool, UK. [3]Dept of Respiratory Medicine, Alder Hey Children's Hospital, Liverpool, UK. [4]Academic Unit, Primary Care and Population Sciences, University of Southampton, Aldermoor Health Centre, Southampton, UK. [5]Centre for Academic Primary Care, Population Health Sciences, Bristol Medical School, Bristol, UK.

Corresponding author: Kay Wang (kay.wang@phc.ox.ac.uk)

Shareable abstract (@ERSpublications)
This trial did not find evidence that early co-amoxiclav use reduces reconsultation due to clinical deterioration in "at risk" children who present with influenza-like illness during influenza season
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Abstract

Introduction The UK government stockpiles co-amoxiclav to treat bacterial complications during influenza pandemics. This pragmatic trial examines whether early co-amoxiclav use reduces reconsultation due to clinical deterioration in "at risk" children presenting with influenza-like illness (ILI) in primary or ambulatory care.

Methods "At risk" children aged from 6 months to 12 years presenting within 5 days of ILI onset were randomly assigned to oral co-amoxiclav 400/57 or a placebo twice daily for 5 days (dosing based on age±weight). "At risk" groups included children with respiratory, cardiac and neurological conditions. Randomisation was stratified by region and used a non-deterministic minimisation algorithm to balance age and current seasonal influenza vaccination status. Our target sample size was 650 children which would have allowed us to detect a reduction in the proportion of children reconsulting due to clinical deterioration from 40% to 26%, with 90% power and 5% two-tailed alpha error (including allowance for 25% loss to follow-up and an inflation factor of 1.041). Participants, caregivers and investigators were blinded to treatment allocation. Intention-to-treat analysis included all randomised participants with primary outcome data on reconsultation due to clinical deterioration within 28 days. Safety analysis included all randomised participants. Trial registration: ISRCTN 70714783. EudraCT 2013-002822-21.

Results We recruited 271 children between February 11, 2015 and April 20, 2018. Primary outcome data were available for 265 children. Only 61 out of 265 children (23.0%) reconsulted due to clinical deterioration. No evidence of a treatment effect was observed for reconsultation due to clinical deterioration (33 out of 133 for co-amoxiclav (24.8%) and 28 out of 132 (21.2%) for placebo; adjusted risk ratio (RR) 1.16, 95% confidence interval (CI) 0.75–1.80). There was also no evidence of a difference between groups in the proportion of children for whom one or more adverse events (AEs) were reported (32 out of 136 (23.5%) for co-amoxiclav and 22 out of 135 (16.3%) for placebo; adjusted RR 1.45, 95% CI 0.90–2.34). In total, 66 AEs were reported (co-amoxiclav, n=37; placebo, n=29). Nine serious AEs were reported per group, although none were considered related to study medication.

Conclusion Our trial did not find evidence that treatment with co-amoxiclav reduces risk of reconsultation due to clinical deterioration in "at risk" children who present early with ILI during influenza season. Our findings therefore do not support early co-amoxiclav use in children with seasonal ILI.