EPIDEMIOLOGY

Long term effects of antenatal betamethasone on lung function: 30 year follow up of a randomised controlled trial

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Background: Antenatal betamethasone is routinely used for the prevention of neonatal respiratory distress syndrome in preterm infants. However, little is known of the long term effects of exposure to antenatal betamethasone on lung function in adulthood.
Methods: Five hundred and thirty four 30 year olds whose mothers had participated in the first and largest randomised controlled trial of antenatal betamethasone were followed. Lung function was assessed by portable spirometric testing. The prevalence of asthma symptoms was assessed using the European Community Respiratory Health Survey questionnaire.
Results: Fifty (20%) betamethasone exposed and 53 (19%) placebo exposed participants met the criteria for current asthma (relative risk 0.98 (95% CI 0.74 to 1.30), p = 0.89). 181 betamethasone exposed and 202 placebo exposed participants had acceptable spirometric data. There were no differences in lung function between betamethasone and placebo exposed groups (mean (SD) forced vital capacity in the betamethasone and placebo groups 105.9 (12.0) *v* 106.6 (12.6)% predicted, difference = −0.7 (95% CI −3.2 to 1.8), p = 0.59; mean (SD) forced expiratory volume in 1 second in the betamethasone and placebo groups 98.9 (13.4) *v* 98.5 (13.6)% predicted, difference = 0.3 (95% CI −2.4 to 3.1, p = 0.80)).
Conclusions: Antenatal exposure to a single course of betamethasone does not alter lung function or the prevalence of wheeze and asthma at age 30.

Antenatal glucocorticoids are recommended best practice in the management of preterm labour for the prevention of neonatal respiratory distress syndrome (RDS).[1] Their use results in considerable reduction in RDS, intraventricular haemorrhage, and neonatal mortality in those born preterm.[1 2] Preterm births account for up to 12% of all births,[3] and a large proportion of these infants are exposed to antenatal glucocorticoids.

Exposure of a preterm fetus to antenatal glucocorticoids results in accelerated maturation of the lung and stimulation of surfactant production. However, in animal studies, antenatal glucocorticoids also alter lung structure resulting in thinning of the mesenchyma and a reduction in alveolarisation.[4] Such structural changes may have long term consequences for later lung function—for example, a reduced lung capacity on spirometric testing. However, as the first infants exposed to antenatal glucocorticoids enter adulthood, the long term effects of antenatal glucocorticoids on lung function in adulthood remain unknown.[1 2] A small follow up study of 81 subjects aged 20 years from a randomised controlled trial found greater medication use in the glucocorticoid exposed participants, with the majority of these participants taking medication for allergies or chronic obstructive pulmonary disease. Lung function and the prevalence of respiratory disease were not reported at age 20,[5] but no differences in lung function were noted between the groups at age 10–12.[6] The only other report of long term lung function following antenatal glucocorticoids is from a non-randomised cohort of 130 subjects aged 14 which found no difference between groups.[7]

We followed the neonatal survivors from the first and largest randomised controlled trial of antenatal glucocorticoids (Auckland Steroid Trial)[8] to assess whether antenatal glucocorticoid exposure alters lung function at 30 years of age.

METHODS

Auckland Steroid Trial

The Auckland Steroid Trial and follow up have been described previously.[8 9] Briefly, between December 1969 and February 1974, all women expected to deliver between 24 and 36 weeks at the National Women's Hospital, Auckland, New Zealand were eligible for enrolment unless immediate delivery was indicated. Women were randomised to receive an intramuscular injection of 6 mg betamethasone phosphate and 6 mg betamethasone acetate or a placebo (trial 1). The allocated treatment was repeated 24 hours later if delivery had not occurred. After the first 717 women had enrolled, the dose of betamethasone in the intervention group was doubled (trial 2) to determine if increasing the dose of betamethasone would increase the efficacy of the treatment. Staff enrolling or assessing participants were blind to study allocation. The primary outcome for the trial was neonatal RDS diagnosed by the presence of clinical signs, grunting respiration, and chest retraction present during the first 3 hours after delivery and persisting beyond the first 6 hours, and radiological criteria on the first day of life.[8]

A total of 1142 women were enrolled and delivered 1218 babies (601 betamethasone exposed and 617 placebo exposed). The incidence of RDS was significantly reduced in those infants exposed to betamethasone (53 (9%)) compared with placebo (89 (14%); relative risk 0.61 (95% CI 0.44 to 0.84), p = 0.002). By 28 days of age there were 988 neonatal survivors, 493 betamethasone exposed and 495 placebo exposed.

Abbreviations: FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; PEF, peak expiratory flow; RDS, respiratory distress syndrome

Thirty year follow up

Between February 2002 and December 2003, neonatal survivors were invited to enter the Steroid Follow-up Study.[9] For the 988 neonatal survivors of the Auckland Steroid Trial, information was only available about their sex, date of birth, and mother's surname at the time of delivery. The neonatal survivors were traced using hospital records and publicly available databases. The Auckland regional ethics committee approved the study on behalf of all New Zealand regional ethics committees. Written informed consent was obtained from each participant.

Participants completed a questionnaire recording occupation, education, income, physical activity, alcohol and tobacco consumption, past medical history, and parental medical history. Asthma symptoms were determined using the European Community Respiratory Health Survey.[10] Participants who resided in New Zealand or were returning to New Zealand within the study time frame attended a clinic or were seen in their own home for further investigations, including spirometric testing supervised by trained study nurses using a Microlab ML3500 portable spirometer (Micro Medical Limited, Rochester, UK). Spirometric data were obtained in the absence of recent use of a bronchodilator (8 hours) and of smoking (1 hour), and are expressed as the percentage predicted for height, sex, and age.[11] European Community Coal and Steel prediction equations were used as these are widely used in New Zealand respiratory laboratories and have been shown to be suitable for local populations.[11 12] Study nurses were asked to obtain three blows from a possible maximum of eight attempts, where the variability of forced expiratory volume in 1 second (FEV_1) added to forced vital capacity (FVC) was $\leqslant$5%. The following lung function parameters were recorded: FVC, FEV_1, peak expiratory flow (PEF), flow at 25% and 50% of forced expiratory flow (F25 and F50), and mean forced expiratory flow between 25% and 75% ($FEF_{25–75\%}$).

Spirometric traces were assessed according to the American Thoracic Society (ATS) criteria for acceptability and reproducibility.[13] Those not meeting this standard were excluded from analysis, except that blows of less than 6 seconds were included if a plateau of at least 1 second was obtained on the volume-time curve.

Participants and all members of the Steroid Follow-up Study involved in tracing, recruitment, assessment, and analysis were unaware of the participants' in utero exposure to betamethasone or placebo.

Statistical analyses

Analyses were performed using SAS Version 8.02 software (SAS Institute, Cary, NC) on an intention-to-treat basis. Continuous variables were compared with unpaired *t* tests or Mann-Whitney tests and categorical data with χ^2 tests as appropriate. Variables with skewed distributions were log transformed. If the distribution remained skewed, data are presented as medians. Data are presented as mean (standard deviation (SD)), antilog transformed geometric means (95% confidence levels (CI)), medians (interquartile range (IQR)), or number (percentage). Differences for categorical and normal data are presented as relative risk (95% CI) and difference between means (95% CI), respectively. The potential confounders of sex, ethnicity, trial type, multiple pregnancy, and neonatal RDS status were explored using multiple linear regression. The effect of multiple pregnancy was further explored by analysing singleton infants alone.

RESULTS

Baseline variables

Of the 988 neonatal survivors, 713 (72%) were successfully traced. Forty two (21 betamethasone exposed and 21 placebo exposed) were known to have died between 28 days of age and the 30 year follow up.[9] Of the 946 individuals presumed to be alive at age 30, 534 were subsequently enrolled in the 30 year follow up (56% of those presumed to be alive and 80% of those traced and presumed to be alive). Those who participated in the follow up were more likely to be from a multiple pregnancy, female, and born preterm compared with those presumed to be alive but unavailable for follow up. There was no difference in other perinatal characteristics,

Table 1 Perinatal characteristics of infants with acceptable spirometric data and those presumed to be alive but unavailable for follow up or without acceptable spirometric data at age 30

	Acceptable spirometric data (n = 383)	No acceptable spirometric data (n = 563)	p value
Maternal characteristics			
Multiple pregnancy	56 (15)	57 (10)	0.04
Unplanned premature labour	311 (81)	473 (84)	0.26
Instrumental delivery	207 (54)	302 (54)	0.90
Complicated by hypertension	33 (9)	34 (6)	0.13
Gestational diabetes	5 (1)	8 (1)	0.88
Haemolytic disease	20 (5)	21 (4)	0.27
Median gestational age at entry (days)	233 (217–243)	231 (216–244)	0.91
Median entry/delivery interval (days)	4.1 (1.9–32)	4.6 (1.5–40)	0.50
Trial 1	243 (63)	342 (61)	0.40
Betamethasone treatment	181 (47)	291 (52)	0.18
Neonatal characteristics			
Male	187 (49)	336 (60)	0.001
Median gestational age delivery (days)	245 (232–265)	250 (238–269)	0.04
Term delivery	121 (32)	213 (38)	0.05
Mean birth weight (g)	2341 (730)	2464 (739)	0.01
Birth weight <1500 g	49 (13)	45 (8)	0.02
Mean birth weight z score	−0.40 (0.93)	−0.37 (1.00)	0.63
Birth weight <10th centile	66 (17)	88 (16)	0.51
Fetal distress	54 (14)	78 (14)	0.92
5 min Apgar score >7	298 (78)	449 (80)	0.47
RDS	33 (9)	36 (6)	0.20
RDS, moderate or severe	22 (6)	27 (5)	0.52

Data are n (%), median (IQR), or mean (SD).
RDS, respiratory distress syndrome.

Table 2 Perinatal characteristics of betamethasone and placebo exposed participants with adequate spirometric data at age 30

	Betamethasone (n = 181)	Placebo (n = 202)	p value
Maternal characteristics			
Multiple pregnancy	34 (19)	22 (11)	0.03
Unplanned premature labour	149 (82)	162 (80)	0.60
Instrumental delivery	103 (57)	104 (51)	0.29
Complicated by hypertension	19 (11)	14 (7)	0.21
Gestational diabetes	3 (2)	2 (1)	0.67
Haemolytic disease	7 (4)	13 (6)	0.26
Median gestational age at entry (days)	231 (217–243)	234 (217–243)	0.50
Median entry/delivery interval (days)	3.9 (1.6–35)	4.2 (1.9–32)	0.98
Trial 1	117 (65)	126 (62)	0.65
Smoking during pregnancy	51 (28)	53 (26)	0.67
Smoking during childhood	98 (54)	106 (52)	0.74
History of asthma	34 (19)	34 (17)	0.62
Paternal characteristics			
Smoking during childhood	92 (51)	106 (52)	0.75
History of asthma	25 (14)	18 (9)	0.13
Neonatal characteristics			
Male	96 (53)	91 (45)	0.12
Median gestational age delivery (days)	245 (231–264)	246 (235–266)	0.41
Term delivery	52 (29)	69 (34)	0.25
Mean birth weight (g)	2318 (769)	2361 (694)	0.57
Mean birth weight z score	−0.40 (0.90)	0.39 (0.96)	0.90
Birth weight <10th centile	29 (16)	37 (18)	0.55
Fetal distress	23 (13)	31 (15)	0.46
5 min Apgar score >7	137 (76)	161 (80)	0.35
RDS	11 (6)	22 (11)	0.09
RDS, moderate or severe	6 (3)	16 (8)	0.05

Data are n (%), median (IQR), or mean (SD).
RDS, respiratory distress syndrome.

including betamethasone exposure, between those participating in the follow up and those presumed to be alive but unavailable for follow up.[9]

Four hundred and fifty six participants (85%) underwent spirometric testing, 383 (84%) of whose traces met the criteria for acceptability and reproducibility (181 betamethasone exposed (81%) and 202 placebo exposed (87%), p = 0.11). Nineteen (26%) of the traces that failed to obtain the criteria for acceptability and reproducibility showed a poor start or poor effort, 48 (66%) showed end of test non-acceptability (early termination, glottic closure or cough), and six (8%) showed lack of reproducibility. The mean (SD) age of follow up was 30.6 (0.9) years in the betamethasone exposed participants and 30.6 (1.0) years in the placebo exposed participants who had acceptable spirometric data. There were no differences in perinatal characteristics between those participating in the 30 year follow up who did and did not have acceptable spirometric data. However, when compared with the entire group of those not included (presumed to be alive but unavailable for follow up or without acceptable spirometry), those with acceptable spirometric data were more likely to be from a multiple pregnancy, female, and born preterm (table 1). Those with acceptable spirometric data were also lighter at birth. This difference was due to being born at an earlier gestational age, as both groups had similar birth weight standard deviation (z) scores. There were no significant differences in other perinatal characteristics between those with acceptable spirometric data and those presumed to be alive but unavailable for follow up or without acceptable spirometric data. Of those with acceptable spirometric data, fewer betamethasone exposed participants had suffered from moderate or severe RDS as a neonate, and more were from a multiple pregnancy (table 2). There were no other differences in perinatal or

Table 3 Adult characteristics of betamethasone and placebo exposed participants with adequate spirometric data at age 30

	Betamethasone (n = 181)	Placebo (n = 202)	p value
Ethnicity			
European	136 (75)	146 (72)	
Maori	35 (19)	49 (24)	
Pacific	10 (6)	6 (3)	
Other	0 (0)	1 (0)	0.31
Body size			
Mean height (cm)	171.9 (9.6)	170.0 (9.5)	0.06
Mean weight (kg)	80 (18)	78 (18)	0.39
Mean BMI (kg/m^2)	26.9 (5.2)	26.9 (5.4)	0.90
Mean serum IgE (mmol/l)*	50.8 (40.4 to 63.8)	50.9 (41.2 to 62.9)	0.99
Tobacco use			
Non-smoker	90 (50)	99 (49)	
Former	28 (15)	47 (23)	
Current	63 (35)	56 (28)	0.10

Data are n (%), mean (SD), or *geometric mean (95% CI)

Table 4 Asthma status in betamethasone and placebo exposed participants at age 30

	Betamethasone (n = 253)	Placebo (n = 281)	Relative risk (95% CI)	p value
Asthma diagnosed by doctor in lifetime	68 (27)	77 (27)	0.98 (0.74 to 1.30)	0.89
Wheezing in the last 12 months	89 (35)	93 (33)	1.06 (0.84 to 1.35)	0.61
Current asthma*	50 (20)	53 (19)	1.05 (0.74 to 1.48)	0.79

Data are n (%).
*Positive response to one or more of the following: current use of asthma medications, attack of asthma in the last 12 months, or waking short of breath in last 12 months.[10]

adult characteristics between the betamethasone and placebo exposed participants with acceptable spirometric data (tables 2 and 3).

Asthma

There was no difference between betamethasone exposed and placebo exposed participants in the prevalence of ever being diagnosed with asthma, wheezing in the last 12 months, or of current asthma (participants reporting one or more of the following; taking asthma medications, an asthma attack in the last 12 months, or waking short of breath in the last 12 months) (table 4).[10]

Other respiratory disease

Eighteen (7%) betamethasone exposed and 15 (5%) placebo exposed participants reported a further respiratory diagnosis in response to the question ''Do you have (or have you had) any other medical conditions?'' These were equally distributed between pneumonia, upper airway conditions, and bronchitis. A spontaneous pneumothorax was reported by one betamethasone exposed and one placebo exposed participant. There was no difference between betamethasone exposed and placebo exposed participants in those who reported an attack of shortness of breath at any time in the previous 12 months (81 (32%) betamethasone exposed and 88 (31%) placebo exposed, relative risk 1.03 (95% CI 0.67 to 1.39), $p = 0.84$).

Lung function

No differences between betamethasone and placebo exposed participants were noted in lung function measurements at age 30 (table 5). Exclusion of current asthmatics and adjustment for ethnicity, multiple pregnancies, trial type (betamethasone dose), and neonatal RDS status did not change these results (data not shown).

DISCUSSION

We studied 534 neonatal survivors at 30 years of age from the first and largest randomised controlled trial of antenatal betamethasone for the prevention of neonatal RDS. We found that antenatal exposure to betamethasone in the doses used in this study did not alter lung function or prevalence of wheeze and asthma at 30 years of age.

Our study is the first to report long term lung function in adulthood following exposure to antenatal betamethasone. The data are consistent with three smaller studies conducted in childhood and early adolescence that also found no difference between betamethasone and placebo exposed groups,[6 7 14] and also with follow up of children exposed to postnatal glucocorticoids.[15] The only other report of outcome in adulthood following exposure to antenatal glucocorticoids was from a study of 81 participants at a mean age of 20.[5] That study found greater medication use in the glucocorticoid exposed group, with the majority of participants taking medication for allergies or chronic obstructive pulmonary disease. This is in contrast to our finding in this much larger study where we found no difference in the prevalence of asthma (including no difference in medication use) or the prevalence of wheeze, raising the possibility that the previous findings may have represented a type 1 error. Our findings in relation to wheeze and asthma are particularly robust as the prevalence found in our study is similar to that reported in longitudinal and cross sectional studies conducted locally in young adults using the same definitions.[16] Post hoc calculations indicate that our study had 80% power ($\alpha = 0.05$) to detect a difference between treatment groups of 3–4% for values of FVC and FEV_1.

Studies in a number of animal species have demonstrated structural changes in the lung following antenatal betamethasone treatment. In particular, antenatal glucocorticoids have been reported to decrease alveolar wall thickness, decrease alveolar numerical density, and increase alveolar volume. These changes have been shown to be dependent on the developmental stage of lung maturation during which exposure occurred, and to be reversible if delivery is delayed until term following exposure early in the third trimester.[17–19] Unfortunately, these studies have involved glucocorticoid exposure either early in gestation[17] or over prolonged periods[18 19] and have not reported long term findings into adulthood. Nevertheless, there is the possibility that

Table 5 Lung function in betamethasone and placebo exposed participants at age 30

	Betamethasone (n = 181)	Placebo (n = 202)	Difference between groups	p value
Mean FVC	105.9 (12.0)	106.6 (12.6)	−0.7 (−3.2 to 1.8)	0.59
Mean FEV_1	98.9 (13.4)	98.5 (13.6)	0.3 (−2.4 to 3.1)	0.80
Mean FEV_1/FVC	0.80 (0.08)	0.79 (0.08)	0.01 (−0.01 to 0.02)	0.48
Mean PEF	101.3 (14.3)	99.1 (15.4)	2.2 (−0.8 to 5.2)	0.15
Mean F50	80.1 (23.2)	77.1 (22.3)	3.0 (−1.5 to 7.6)	0.19
Mean F25	64.0 (20.5)	63.6 (21.6)	0.4 (−3.8 to 4.7)	0.84
Mean $FEF_{25–75\%}$	74.9 (21.6)	72.7 (21.3)	2.2 (−2.1 to 6.5)	0.31
FEV_1/FVC <70%	18 (10)	23 (11)	0.87 (0.49 to 1.57)	0.65

FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 second; PEF, peak expiratory flow; F50, F25, flow at 50% and 25% of forced expiratory flow; $FEF_{25–75}$, mean forced expiratory flow between 25% and 75%.
Data are mean (SD) or n (%). Differences between groups are differences between means (95% CI) or relative risk (95% CI).
Data are percentage predicted adjusted for sex and height.[11]

structural changes induced by antenatal glucocorticoids in the perinatal period may have a long term effect on the later lung function of exposed infants.

Clinicians should be reassured by the findings of this study that exposure to antenatal glucocorticoids in the doses used in this trial—and which remain those recommended in current clinical practice[1 20]—cause no changes in lung function or prevalence of wheeze and asthma at age 30. These findings were unaffected by whether the participant was exposed to the lower or higher dose of betamethasone (trial 1 or trial 2). The effects of betamethasone on neonatal outcomes were similarly unaffected by the different doses used.

Unfortunately, this reassurance cannot be extended to repeat courses of antenatal glucocorticoids. Such courses have been widely administered, often weekly, when a fetus remains undelivered but still at risk of preterm delivery 7 days after the initial course of antenatal glucocorticoids, since the benefits of a single course appear to wane after this time.[2 21] Animal studies of repeat courses of glucocorticoids have demonstrated improvements in lung function at birth, but at the cost of significantly decreased overall fetal growth.[22] In sheep, changes in lung structure are more pronounced after repeat courses of glucocorticoids, with increasing alveolar volume and decreasing alveolar numerical density.[19] Thus, notwithstanding our reassuring findings, future long term follow up of lung function into adulthood will be important for participants in recent and ongoing randomised trials of repeat doses of antenatal glucocorticoids.

There are a number of limitations to our study. Firstly, only 56% of neonatal survivors presumed to be alive participated. However, incomplete follow up would only bias our results if the association between betamethasone exposure and adult lung function differed between those followed up and those who did not participate in the follow up study. Although we cannot exclude this possibility, since the original trial was randomised, there is no reason to think this might be the case.

Secondly, only 73 participants (14%) were born at <1500 g or <30 weeks gestation and the results of this study should therefore be interpreted with caution with respect to these smaller babies. However, the majority of both preterm babies and infants exposed to antenatal glucocorticoids are born at more than 30 weeks gestation. Thus, our findings remain very relevant to current practice.

Thirdly, information on neonatal chronic lung disease was not collected in the original trial. However, chronic lung disease following prolonged ventilation for neonatal RDS had only just been described by Northway[23] and was still very uncommon at the time that our cohort was born. Furthermore, antenatal glucocorticoids have not been shown to affect rates of neonatal chronic lung disease.[2] Since there were similar numbers of neonatal survivors with similar perinatal morbidity in both treatment groups, possible differences in chronic lung disease between groups is most unlikely to have influenced our findings regarding the long term effects of antenatal betamethasone.

Finally, detailed assessment of alveolarisation, by measurement either of diffusing capacity for carbon monoxide or of compliance, was not feasible in this study because of the large geographical spread of participants. However, FVC (an indirect measure of alveolarisation) did not differ between treatment groups, nor was there any difference in the number of participants reporting an attack of shortness of breath at any time in the previous 12 months.

We conclude that exposure to antenatal betamethasone in currently recommended doses has no apparent effect on lung function or prevalence of wheeze and asthma 30 years later. A single course of antenatal glucocorticoids for the prevention of neonatal RDS significantly reduces rates of neonatal RDS and mortality.[1 2] We therefore recommend that the current practice of administering antenatal glucocorticoids for the prevention of neonatal RDS should continue.

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LUNG ALERT

A novel form of receptor interaction may contribute to β-agonist resistance in asthma

▲ McGraw DW, Mihlbachler KA, Schwarb MR, *et al*. Airway smooth muscle prostaglandin-EP_1 receptors directly modulate β_2-adrenergic receptors within a unique heterodimeric complex. *J Clin Invest* 2006;**116**:1400–9

In attempting to elucidate the hitherto poorly understood action of the prostanoid-EP_1 receptor, researchers in the US have uncovered a new type of receptor interaction and demonstrated its action on murine airway smooth muscle contraction.

Prostaglandin E_2 (PGE_2) produces its diverse biological effects by acting on four endogenous receptor subtypes (EP_1–EP_4). The authors set out to define the action of the EP_1 receptor. In a series of experiments they first showed that activation of EP_1 receptors by PGE_2 failed to cause contraction of mouse tracheal ring, as might have been expected, but did cause a marked reduction in β_2 adrenergic receptor (β_2AR) mediated relaxation. This was shown to be mediated at the level of the receptor itself. This suggested an interplay between the EP_1 receptor and the β_2AR, with activation of the former resulting in decreased function of the latter. They went on to demonstrate coupling of the two receptors into a heterodimer. Activation of the EP_1 receptor within the heterodimer causes a conformational change in the β_2AR, uncoupling it from its G protein with resultant desensitisation to β_2AR agonists.

This study demonstrates a novel modulatory function of the EP_1 receptor in regulating the action of the β_2AR. This may contribute to the reduced response to β_2AR agonists in severe asthma, when there may be increased concentrations of endogenous PGE_2.

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LUNG ALERT

Short course antibiotics in community acquired pneumonia

▲ El Moussaoui R, de Borgie CA, van den Broek P, *et al*. Effectiveness of discontinuing antibiotic treatment after three days versus eight days in mild to moderate-severe community acquired pneumonia: randomised, double blind study. *BMJ* 2006;**332**:1355–8

This Dutch study, undertaken between November 2000 and July 2003, took adults with a pneumonia severity index score of $\leqslant 110$ and randomly assigned those who substantially improved after 72 hours of intravenous amoxicillin to either 750 mg oral amoxicillin (n = 63) or placebo (n = 56) three times daily for 5 days thereafter.

Clinical, bacteriological and radiological outcomes were assessed. The clinical success rate at day 10 (per protocol analysis) was 93% in both groups (50/54 in the 3 day treatment group and 56/60 in the 8 day treatment group: difference 0.1% (95% CI −9 to 10)). At day 28 clinical success rates were 90% (47/52) in the 3 day treatment group and 88% (49/56) in the 8 day treatment group (difference 2% (95% CI −9 to 15)). There was therefore little difference between the two groups.

This study suggests that a short course of antibiotic therapy is not inferior to a longer course in patients with mild to moderate-severe uncomplicated community acquired pneumonia who show clinical improvement after 3 days of intravenous antibiotics.

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