Do patients presenting to primary care with LRTI at increased risk of a poor outcome benefit from treatment with amoxicillin?

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Team

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Background

Acute cough

→ one of the main reasons for consulting in primary care

→ usually caused by self limiting LRTI

Antibiotics prescribed to >50% of acute cough cases[1]

→ limited benefit in uncomplicated LRTI[2]

→ limited benefit in clinical high-risk subgroups[3]

➔ benefit in etiological high-risk subgroups?

1. Butler *et al.* BMJ 2009;338:b2242; 2. Little *et al.* LID 2013;13:123-9; 3. Moore *et al.* BJGP 2014;64:e75-80.

Study aim

Evaluate the benefit of amoxicillin treatment

in acute LRTI patients with:

- confirmed bacterial infection
- confirmed viral infection
- confirmed combined infection (bacterial + viral)
- elevation of C-reactive protein (CRP)
- elevation of procalcitonin (PCT)
- elevation of blood urea nitrogen (BUN)

Definitions

Bacterial:

Streptococcus pneumoniae, *Haemophilus influenzae*, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Bordetella pertussis* or *Legionella pneumoniae* → excluding bacteria that are natively present

Viral:

rhinovirus, influenza, coronavirus, respiratory syncytial virus, human metapneumovirus, parainfluenza virus, adenovirus, polyomavirus or bocavirus

Data

GRACE: Genomics to combat Resistance against Antibiotics in Community-acquired LRTI in Europe

Work package 10a[1]:

→ 2058 non-pregnant adults (>18 years) with acute LRTI

→ recruited in 2007-2010 from 12 European countries

→ not treated with antibiotics in last month

→ randomized to either placebo or amoxicillin (1g)

1. Little *et al.* LID 2013;13:123-9.

Sample composition

	Number of patients (%)
ANY: bacterial or viral	1310 (63.4%)
BACT: bacterial	425 (20.7%)
BACT ONLY	226 (11.0%)
VIR: viral	1010 (49.1%)
VIR ONLY	811 (39.4%)
BACT AND VIR	199 (9.7%)
PCT high	484 (23.5%)
Urea high	483 (23.5%)
CRP high	484 (23.5%)

Main outcomes

- Symptom duration:

duration of symptoms rated moderately bad or worse

→ score ≥ 3

- Symptom severity:

mean symptom score on days 2-4

- Illness deterioration:

reconsultation with new or worsened complaints or admission to hospital

Analyses

- Symptom duration

  → survival outcome: Cox regression

- Symptom severity

  → continuous outcome: linear regression

- Illness deterioration

  → binary outcome: logistic regression

➔ Benefit of treatment in subgroups:

interaction treatment - subgroup

Results: symptom duration

	Interaction term		Within subgroup	
	HR 95%CI	p-value	HR 95%CI	p-value
Whole cohort			1.06 (0.96 – 1.17)	0.268
ANY: BACT OR VIR	0.92 (0.75 – 1.14)	0.435	1.03 (0.91 – 1.16)	0.673
BACT	0.96 (0.76 – 1.23)	0.767	1.03 (0.83 – 1.27)	0.821
BACT ONLY	1.10 (0.80 – 1.51)	0.554	1.13 (0.84 – 1.53)	0.421
VIR	0.92 (0.75 – 1.12)	0.394	1.01 (0.88 – 1.17)	0.884
VIR ONLY	0.98 (0.80 – 1.21)	0.855	1.04 (0.89 – 1.23)	0.599
BACT AND VIR	0.83 (0.59 – 1.15)	0.250	0.89 (0.65 – 1.21)	0.450
PCT high	1.06 (0.84 – 1.34)	0.602	1.09 (0.89 – 1.33)	0.423
Urea high	0.96 (0.76 – 1.21)	0.723	0.99 (0.81 – 1.22)	0.956
CRP high	1.03 (0.81 – 1.31)	0.797	1.06 (0.86 – 1.31)	0.567

➔ Amoxicillin treatment does not affect duration of symptoms

Results: symptom severity

	Interaction term		Within subgroup	
	MD 95%CI	p-value	MD 95%CI	p-value
Whole cohort			-0.07 (-0.15 – 0.01)	0.065
ANY: BACT OR VIR	0.03 (-0.13 – 0.19)	0.720	-0.06 (-0.16 – 0.04)	0.221
BACT	-0.09 (-0.28 – 0.10)	0.330	-0.14 (-0.31 – 0.03)	0.108
BACT ONLY	-0.25 (-0.49 – 0.003)	0.048	-0.26 (-0.48 - -0.03)	0.027
VIR	0.12 (-0.03 – 0.28)	0.119	-0.02 (-0.13 – 0.10)	0.801
VIR ONLY	0.09 (-0.07 – 0.25)	0.251	-0.02 (-0.15 – 0.11)	0.755
BACT AND VIR	0.10 (-0.15 – 0.36)	0.423	-0.01 (-0.27 – 0.25)	0.943
PCT high	-0.09 (-0.27 – 0.09)	0.326	-0.13 (-0.30 – 0.04)	0.144
Urea high	-0.03 (-0.21 – 0.16)	0.782	-0.08 (-0.23 – 0.07)	0.294
CRP high	-0.07 (-0.25 – 0.12)	0.473	-0.12 (-0.29 – 0.06)	0.201

➔ Amoxicillin treatment does not affect symptom severity

Results: odds of illness deterioration

	Interaction term		Within subgroup	
	OR 95%CI	p-value	OR 95%CI	p-value
Whole cohort			0.80 (0.63 – 1.00)	0.051
ANY: BACT OR VIR	0.58 (0.36 – 0.95)	0.029	0.67 (0.50 – 0.88)	0.005
BACT	0.47 (0.27 – 0.82)	0.007	0.46 (0.29 – 0.75)	0.002
BACT ONLY	0.91 (0.46 – 1.79)	0.792	0.75 (0.40 – 1.40)	0.364
VIR	0.66 (0.41 – 1.04)	0.075	0.64 (0.46 – 0.90)	0.010
VIR ONLY	1.12 (0.69 – 1.81)	0.639	0.87 (0.59 – 1.27)	0.464
BACT AND VIR	0.26 (0.11 – 0.59)	0.001	0.24 (0.11 – 0.53)	<0.001
PCT high	0.62 (0.36 – 1.06)	0.079	0.55 (0.35 – 0.86)	0.010
Urea high	1.15 (0.67 – 1.99)	0.605	0.88 (0.55 – 1.41)	0.593
CRP high	1.03 (0.60 – 1.75)	0.927	0.80 (0.51 – 1.27)	0.350

➔ Amoxicillin treatment affects odds of illness deterioration

→ Number needed to treat = 4.55

Discussion

Amoxicillin treatment:

→ no reduction in symptom severity or duration

→ decreased odds of illness deterioration

ONLY FOR combined infections

→ identification of pathogens takes time

→ could be faster through POCT

When considering antibiotics, balance:

→ side-effects and resistance

→ limited benefit

THANKS

for your attention!

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