

Summary of findings:

23. Antibiotics compared to placebo for acute otitis media - short term outcomes

Patient or population: Children aged 2 months to 12 years with acute otitis media

Setting: Primary health care

Intervention: Antibiotics (Studies used: amoxicillin 40-90mg/kg/day three times daily, amoxicillin with clavulanate 40-90 / 5.7-6.4mg/kg/day twice daily, ampicillin 100 mg/kg/day four times daily, phenoxymethyl penicillin 50 mg/kg/day twice daily and penicillin 500-1500mg/day four times daily with dose adjusted with age. Duration was from 5-14 days.)

Comparison: Placebo

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Antibiotics	With Antibiotics	Difference		
Pain assessed with: parental report +/- clinical assessment follow up: median 24 hours № of participants: 1394 (6 RCTs) ^{1,b,c}	RR 0.89 (0.78 to 1.01)	42.6%	37.9% (33.2 to 43.1)	4.7% fewer (NS) (9.4 fewer to 0.4 more)	⊕⊕⊕⊕ HIGH	In children with AOM treated with antibiotics compared to placebo there is no reduction in pain at 24 hours. NNT Not Applicable
Pain assessed with: parental report +/- clinical assessment follow up: range 2 to 3 days № of participants: 2320 (7 RCTs) ^{1,b,d}	RR 0.70 (0.57 to 0.86)	15.9%	11.1% (9.0 to 13.7)	4.8% fewer (6.8 fewer to 2.2 fewer)	⊕⊕⊕○ MODERATE ^e	In children with AOM treated with antibiotics compared to placebo there is probably a reduction in pain at 2-3 days. NNT ~21
Pain assessed with: parental report +/- clinical assessment follow up: range 4 to 7 days № of participants: 1347 (8 RCTs) ^{1,b,f}	RR 0.76 (0.63 to 0.91)	24.1%	18.3% (15.2 to 22.0)	5.8% fewer (8.9 fewer to 2.2 fewer)	⊕⊕⊕○ MODERATE ^e	In children with AOM treated with antibiotics compared to placebo there is probably a reduction in pain at 4-7 days. NNT ~18
Pain assessed with: parental report +/- clinical assessment follow up: range 10 to 12 days № of participants: 278 (1 RCT) ^{1,b,g}	RR 0.33 (0.17 to 0.66)	21.6%	7.1% (3.7 to 14.2)	14.5% fewer (17.9 fewer to 7.3 fewer)	⊕⊕○○ LOW ^{e,h}	In children with AOM treated with antibiotics compared to placebo there is possibly a reduction in pain at 10-12 days. NNT ~7

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Comparison: Placebo

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Antibiotics	With Antibiotics	Difference		
Adverse events (vomiting, diarrhoea or rash) assessed with: parental report follow up: range 7 days to 4 weeks № of participants: 2107 (8 RCTs) ^{1,j}	RR 1.38 (1.19 to 1.59)	19.6%	27.0% (23.3 to 31.1)	7.4% more (3.7 more to 11.5 more)	HIGH	In children with AOM treated with antibiotics compared to placebo there is more adverse events during 4 weeks follow-up. NNH ~14
Tympanic membrane perforation assessed with: otoscopy follow up: range 7 days to 4 weeks № of participants: 1075 (5 RCTs) ^{1,j}	RR 0.37 (0.18 to 0.76)	4.8%	1.8% (0.9 to 3.6)	3.0% fewer (3.9 fewer to 1.2 fewer)	MODERATE ^e	In children with AOM treated with antibiotics compared to placebo there is probably fewer tympanic membrane perforations during 4 weeks follow-up. NNT ~34

Treatment failure (lack of substantial improvement, worsening of otoscopic signs, worsening clinical condition at any time)

Proportion of children > 2 years of age with unilateral AOM (№ of participants: 611; 6 RCTs) ^{2,l,k}

RR 0.92
(0.85 to 1.01)

26.2% ^m

24.1%
(22.3 to 26.5) ^m

2.1% fewer (NS)
(3.9 fewer to 0.3
more)


MODERATE ^e

In children >2 years with unilateral AOM treated with antibiotics compared to placebo there is probably no difference in treatment failure at 3-5 days follow-up.


NNT Not Applicable

Assessed with: parental report +/- clinical


Proportion of children <2 years (№ of participants: 567; 6 RCTs) ^{2,l,k,m}


assessment	RR 0.77 (0.68 to 0.89)	47.6% ^m	36.6% (32.3 to 42.3) ^m	10.9% fewer (15.2 fewer to 5.2 fewer)	 MODERATE ^e	In children <2 years treated with antibiotics compared to placebo there is probably fewer treatment failures during 3-5 days follow-up.
Follow up: range 3 to 5 days						NNT ~10

Proportion of children with bilateral AOM at diagnosis (№ of participants: 456; 6 RCTs)^{2,i,k}

	RR 0.72 (0.62 to 0.84)	47.5% ^m	34.2% (29.4 to 39.9) ^m	13.3% fewer (18 fewer to 7.6 fewer)	 MODERATE ^e	In children with bilateral AOM treated with antibiotics compared to placebo there is probably fewer treatment failures during 3-5 days follow-up.
						NNT ~8

Proportion of children with otorrhoea through TM perforations at diagnosis (№ of participants: 116; 6 RCTs)^{2,k,l}

	RR 0.52 (0.37 to 0.73)	60.0% ^m	31.2% (22.2 to 43.8) ^m	28.8% fewer (37.8 fewer to 16.2 fewer)	 MODERATE ^e	In children with AOM and otorrhoea at diagnosis treated with antibiotics compared to placebo there is probably fewer treatment failures at 3-5 days follow-up.
						NNT ~4

Proportion of children >2 years of age with treatment failure assessed with: pain, fever or both follow up: range 3 to 7 days № of participants: 1076 (6 RCTs) ^{2,j}	RR 0.86 (0.80 to 0.93)	30.9%	26.6% (24.7 to 28.7)	4.3% fewer (6.2 fewer to 2.2 fewer)	 MODERATE ^e	In children >2 years with AOM treated with antibiotics compared to placebo there is probably fewer treatment failures at 3-7 days follow-up.
						NNT ~24

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio; NS: Not significant; NNT: Number needed to treat; NNH: Number needed to harm; MD: Mean difference

GRADE Working Group grades of evidence

High quality: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

- a. Studies include amoxicillin alone, amoxicillin with clavulanate, and penicillin
- b. Proportion of children with any pain at timepoint - various instruments across studies
- c. Studies taken from: Cochrane Review, Venekamp 2015 (Burke 1991, Le Saux 2005, Thalín 1985, Tahtinen 2011, van Buchem 1981a, van Buchem 1981b)
- d. Studies taken from: Cochrane Review, Venekamp 2015 (Appleman 1991, Halsted 1968, Kaleida 1991, Le Saux 2005, Mygind 1981, Thalín 1985, Tahtinen 2011)
- e. Imprecision: Optimal information size not reached
- f. Studies taken from: Cochrane Review, Venekamp 2015 (Burke 1991, Damoiseaux 2000, Mygind 1981, Tapiainen 2014, Thalín 1985, Tahtinen 2011, van Buchem 1981a, van Buchem 1981b)
- g. Studies taken from: Cochrane Review, Venekamp 2015 (Hoberman 2011)
- h. Indirectness: Timepoint not specified a priori as an outcome of interest
- i. Studies taken from: Cochrane Review, Venekamp 2015 (Burke 1991, Damoiseaux 2000, Hoberman 2011, Le Saux 2005, Mygind 1981, Tapiainen 2014, Thalín 1985, Tahtinen 2011)
- j. Studies taken from: Cochrane Review, Venekamp 2015 (Tapiainen 2014, Hoberman 2011, Tahtinen 2011, Burke 1991, Mygind 1981)

- k. Treatment failure - composite outcome of persisting pain and or fever, worsening of otoscopic signs, and/or deterioration of patient's overall condition
- l. Studies taken from: Rovers meta-analysis with individual patient data (Appleman 1991, Burke 1991, Damoiseaux 2000, Little 2001, Le Saux 2005, McCormick 2005)
- m. Some data estimated from published data
- n. Note: Hoberman 2011, Tahtinen 2011 - <2 year old children, strict diagnostic criteria

References

1. Venekamp RP, Sanders SL, Glasziou PP, Del Mar CB, Rovers MM. Antibiotics for acute otitis media in children. The Cochrane database of systematic reviews. 2015(6):Cd000219. Epub 2015/06/24. doi: 10.1002/14651858.CD000219.pub4. PubMed PMID: 26099233.
2. Rovers MM, Glasziou P, Appelman CL, Burke P, McCormick DP, Damoiseaux RA, et al. Antibiotics for acute otitis media: a meta-analysis with individual patient data. *Lancet* (London, England). 2006;368(9545):1429-35. Epub 2006/10/24. doi: 10.1016/s0140-6736(06)69606-2. PubMed PMID: 17055944.