

Summary of findings:





27. Azithromycin compared to Amoxicillin with or without clavulanate for acute otitis media

Patient or population: Children aged 3 months to 15 years old with acute otitis media.

Setting: Primary health care.

Intervention: Azithromycin (Studies used: 30-60mg/kg (60mg/kg extended release tablet)) Duration was a single stat dose or daily for 3-6 days.

Comparison: Amoxicillin with or without clavulanate (Studies used: 40-90mg/kg/day two to three divided doses daily.) Duration was for 7-10 days.

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Azithromycin	With Azithromycin	Difference		
Treatment failure assessed by: clinical and otoscopic assessment. follow up: ≤1 months № of participants: 5150 (19 RCTs) ^{1,2,3,4,a}	RR 0.99 (0.89 to 1.11)	22.0%	21.8% (19.6 to 24.4)	0.2% fewer (NS) (2.4 fewer to 2.4 more)	 MODERATE ^b	In children with AOM treated with Azithromycin compared to Amoxicillin+/- clavulanate there is probably no reduction in treatment failure during 1 month follow-up. NNT Not Applicable
Treatment failure assessed by: clinical and otoscopic assessment. follow up: range 8 to 19 days № of participants: 5274 (19 RCTs) ^{1,2,3,4,a}	RR 1.18 (0.98 to 1.43)	12.5%	14.8% (12.3 to 17.9)	2.3% more(NS) (0.3 fewer to 5.4 more)	 MODERATE ^b	In children with AOM treated with Azithromycin compared to Amoxicillin+/- clavulanate there is probably no reduction in treatment failure during 8-19 days follow-up. NNT Not Applicable
Treatment failure (Single dose Azithromycin compared to longer course Amoxicillin+/- clavulanate) assessed by: clinical and otoscopic assessment. follow up: ≤1 months № of participants: 1320 (4 RCTs) ^{2,3,4,c}	RR 0.95 (0.80 to 1.12)	26.9%	25.6% (21.5 to 30.2)	1.3% fewer(NS) (5.4 fewer to 3.2 more)	 MODERATE ^d	In children with AOM treated with single dose Azithromycin compared to Amoxicillin+/- clavulanate there is probably no reduction in treatment failure during 1 month follow-up. NNT Not Applicable
Treatment failure by end of therapy in remote Aboriginal children assessed by: video pneumatic otoscopy, tympanometry follow up: range 6 to 11 days № of participants: 320 (1 RCT) ^{3,e}	RR 0.93 (0.75 to 1.15)	53.5%	49.8% (40.2 to 61.6)	3.7% fewer(NS) (13.4 fewer to 8 more)	 MODERATE ^f	In remote Australian Aboriginal Children with AOM treated with single dose Azithromycin compared to Amoxicillin there is probably no reduction in treatment failure at 6-11 days follow-up. NNT Not Applicable.

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Outcome No of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without Azithromycin	With Azithromycin	Difference		
Adverse effects (gastrointestinal) assessed by: parental report follow up: median 1 months No of participants: 5269 (16 RCTs) ^{2,3,4,g}	RR 0.59 (0.52 to 0.68)	17.9%	10.5% (9.3 to 12.1)	7.3% fewer (8.6 fewer to 5.7 fewer)	 LOW ^{b,h}	In children with AOM treated with Azithromycin compared to Amoxicillin+/- clavulanate there are possibly fewer gastrointestinal adverse effects during 1 month follow-up. NNT ~14

*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

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 taken from: (1) Cochrane Review, Kozyrskij 2010 (Arguedas 1996, 2005, Aronovitz 1996, Arrieta 2003, Block 2003, Dagan 2000, Daniel 1993, de Jose 1998, Dunne 2003, Guven 2006, Hoberman 2005, Khurana 1996, McLinn 1996, Mohs 1993, Petalozza 1992, Principi 1995, Schaad 1993); (2) Courter Meta-Analysis 2010 (McLinn 1996, Block 2003, Dagan 2000, Dunne 2003, Guven 2006, Hoberman 2005, Arguedas 2005); (3) Morris 2010, (4) Arguedas 2011
- b. Risk of bias: selection and performance bias (several studies)
- c. Studies taken from: (1) Cochrane Review, Kozyrskij 2010 (Arguedas 2005, Block 2003); (2) Morris 2010, (3) Arguedas 2011
- d. Risk of Bias: Interim analysis (selective reporting bias) (Arguedas 2005)
- e. Study: Morris 2010
- f. Imprecision: Small study, not powered to detect equivalence
- g. Studies taken from: (1) Cochrane Review, Kozyrskij 2010 (Arguedas 1996, 2005, Arrieta 2003, Block 2003, Dagan 2000, Daniel 1993, de Jose 1998, Guven 2006, Khurana 1996, McLinn 1996, Mohs 1993, Petalozza 1992, Principi 1995, Schaad 1993); (2) Morris 2010, (3) Arguedas 2011
- h. Inconsistency: High heterogeneity

References

1. Courter JD, Baker WL, Nowak KS, Smogowicz LA, Desjardins LL, Coleman CI, et al. Increased clinical failures when treating acute otitis media with macrolides: a meta-analysis. *The Annals of pharmacotherapy*. 2010;44(3):471-8. Epub 2010/02/13. doi: 10.1345/aph.1M344. PubMed PMID: 20150506.
2. Kozyrskij A, Klassen TP, Moffatt M, Harvey K. Short-course antibiotics for acute otitis media. *The Cochrane database of systematic reviews*. 2010(9):Cd001095. Epub 2010/09/09. doi: 10.1002/14651858.CD001095.pub2. PubMed PMID: 20824827.

3. Morris PS, Gadil G, McCallum GB, Wilson CA, Smith-Vaughan HC, Torzillo P, et al. Single-dose azithromycin versus seven days of amoxicillin in the treatment of acute otitis media in Aboriginal children (AATAAC): a double blind, randomised controlled trial. *The Medical journal of Australia*. 2010;192(1):24-9. Epub 2010/01/06. PubMed PMID: 20047544.
4. Arguedas A, Soley C, Kamicker BJ, Jorgensen DM. Single-dose extended-release azithromycin versus a 10-day regimen of amoxicillin/clavulanate for the treatment of children with acute otitis media. *International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases*. 2011;15(4):e240-8. Epub 2011/01/29. doi: 10.1016/j.ijid.2010.12.003. PubMed PMID: 21269858.