

Efficacy and safety of clarithromycin in pediatric patients with upper respiratory infections: a systematic review with meta-analysis

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ABSTRACT

Purpose. Upper respiratory infections (URIs) are one of the most common infectious diseases in children. Macrolides had been considered one of the best options of treatment. Instead of clarithromycin is one of the macrolides most used, meta-analysis about the safety and efficacy of this drug has not been published. **Materials and methods.** A systematic review with meta-analysis of randomized controlled trials (RCTs) was conducted. Studies in subjects ≤ 12 years of age with URIs were included. Central Cochrane Registry, MEDLINE, EMBASE, Lilacs and Artemisa from 1966 to January of 2011 were reviewed. Clinical cure, clinical success, bacteriological eradication, relapse risk and adverse events risks were analyzed. Risks ratios (RR) with 95% confidence intervals (CI 95%) were calculated, using a fixed effects model. **Results.** 24 studies, from a total of 76 RCTs were included. Clarithromycin was therapeutically equivalent to other antibiotics studied with respect to clinical cure [RR 1.02 (0.98 to 1.06), p NS], clinical success [RR 1.01 (0.99 to 1.03), p NS] and relapse risk [RR 1.34 (0.81 to 2.21), p NS], but was associated with a better bacteriological eradication [RR 1.06 (1.02 to 1.09), p 0.001], and a lower risk for related adverse events [RR 0.77 (0.65 to 0.90), p = 0.001]. **Conclusions.** High quality evidence showed that Clarithromycin is a safe and effective alternative for the treatment of URIs in pediatric patients. Is superior to other antibiotics in relation to bacterial eradication. Its equivalence profile related to clinical cure, clinical success and relapse risk, let to consider it as an important alternative.

Key words. Clarithromycin. Upper respiratory infections. Children.

Eficacia y seguridad de la claritromicina en pacientes pediátricos con infecciones respiratorias superiores: una revisión sistemática con metaanálisis

RESUMEN

Justificación. Las infecciones respiratorias (IRAs) son uno de los procesos infecciosos más frecuentes en niños. Los macrolidos se han considerado como una de las mejores opciones para su tratamiento. La claritromicina es el macrolido más utilizado. No se ha publicado ningún metaanálisis sobre la eficacia y seguridad de la claritromicina en niños. **Material y métodos.** Se realizó una revisión sistemática de la evidencia con metaanálisis de ensayos clínicos controlados (RCTs), efectuados en sujetos de ≤ 12 años con IRAs. Se efectuó búsqueda de la evidencia publicada en Central Cochrane Registry, MEDLINE, EMBASE, Lilacs y Artemisa de 1966 a enero 2011. Se analizaron como variables de desenlace la curación clínica, tasa de éxito, erradicación bacteriológica, riesgo de recaída y presencia de eventos adversos. Se efectuó cálculo de razón de riesgos (RR) con intervalo de confianza a 95% (IC95%), utilizando un modelo de efectos fijos. **Resultados.** Se incluyeron 24 estudios de un total de 76 RCTs evaluados. La claritromicina fue equivalente a otros antibióticos en relación con la curación clínica [RR 1.02 (0.98 a 1.06), p NS], tasa de éxito [RR 1.01 (0.99 a 1.03), p NS] y riesgo de recaída [RR 1.34 (0.81 a 2.21), p NS], asociándose con una mayor erradicación bacteriológica [RR 1.06 (1.02 a 1.09), p 0.001], y con un riesgo menor de eventos adversos relacionados [RR 0.77 (0.65 a 0.90), p = 0.001]. **Conclusiones.** La evidencia de calidad demuestra que la claritromicina es una alternativa eficaz y segura para el tratamiento de las IRAs en niños. Es superior a otros antibióticos en relación con la erradicación bacteriana. Su perfil de equivalencia con otros antibióticos para la curación clínica, tasa de éxito y riesgo de recaída la soportan como una alternativa significativa.

Palabras clave. Claritromicina. Infecciones respiratorias. Niños.

BACKGROUND

Acute pharyngitis

Acute pharyngitis, a commonly occurring illness, is responsible for 1 to 2% of all visits to outpatient departments, emergency rooms and physician offices.¹ The etiology includes bacteria, viruses and atypical organisms (i.e. chlamydia, mycoplasma). The most common cause of bacterial pharyngitis is group A beta-hemolytic streptococcus (GABHS) (*Streptococcus pyogenes*), which is responsible for 15-30% and 5-10% of all cases in children and adults, respectively.¹⁻⁴ Antibiotic therapy is recommended for pharyngitis caused by GABHS, but not for any of the other forms of the infection.⁵ Although GABHS pharyngitis is typically self-limiting, antibiotic therapy initiated early in the course of illness can hasten the resolution of clinical symptoms^{1,6,7} and is utilized to prevent the occurrence of non-suppurative sequelae such as rheumatic fever.^{8,9} Penicillin for 10 days is considered the regimen of choice for the treatment of GABHS pharyngitis.^{4,5,10} Other beta-lactams (e.g. ampicillin, amoxicillin, cephalosporins), macrolides and clindamycin, have also been shown to be effective in the management of this infection.⁵ Although a 10-day course of antibiotics is considered standard therapy, data suggest that short course regimens of clarithromycin, azithromycin, or a cephalosporin (e.g. cefuroxime, cefixime, cefdinir, ceftibuten, cefpodoxime) are equally effective.¹¹⁻¹⁷ Obvious advantages to shorter courses include improved adherence, more favorable patient/parent acceptance, and, in some circumstances, decreased direct and indirect costs.^{18,19}

Acute otitis media

Acute otitis media (AOM) is the most common childhood infection for which antibiotics are prescribed in the United States.²⁰⁻²² A study using 2006 Medical Expenditure Panel Survey data demonstrated an average expenditure of \$350 per child with AOM, totaling \$2.8 billion.²³ Timely and accurate diagnosis and appropriate management of AOM may have significant consequences for ambulatory health care utilization and expenditures. Multiple systematic reviews on AOM diagnosis and management have been conducted,²⁴⁻²⁹ including 2001 study by Takata GS³⁰ which was the basis for the 2004 American Academy of Pediatrics and American Academy of Family Physicians joint practice guidelines.³¹ Since then, new trials have been pu-

blished, the heptavalent pneumococcal conjugate vaccine (PCV7) has become widely used, and clinician practice has changed regarding antibiotic choice for AOM.³² Since the introduction of PCV7, there have been significant shifts in AOM microbiology, with *S pneumoniae* becoming less prevalent and *H. influenzae* becoming more prevalent. A recent study of a single pediatric practice found evidence suggesting that this balance may be shifting again because of an increase in the proportion of AOM with nonvaccine *S. pneumoniae* serotypes.³³ These data and the introduction of PCV13 support the need for ongoing surveillance of AOM isolates. Immediate ampicillin/amoxicillin treatment has a modest benefit compared with placebo or delayed antibiotics but also may be associated with more diarrhea and rash. Of 100 average risk children with AOM, approximately 80 would likely get better within about 3 days without antibiotics.³⁴ If all were treated with immediate ampicillin/amoxicillin, an additional 12 would likely improve, but 3 to 10 children would develop rash and 5 to 10 would develop diarrhea. Clinicians need to weigh these risks (including possible long-term effects on antibiotic resistance) and benefits before prescribing immediate antibiotics for uncomplicated AOM. Most antibiotics used to treat uncomplicated AOM in children at normal risk have similar rates of clinical success.

Clarithromycin and upper respiratory infections

Clarithromycin is a new macrolide antibiotic with *in vitro* activity similar to erythromycin.³⁵⁻³⁷ Clarithromycin is effective against a wide range of microorganisms, including Gram-positive cocci, *Haemophilus influenzae*, *Moraxella catarrhalis*, mycoplasma, chlamydia, selected mycobacteria, *Legionella* spp. and protozoan organisms.³⁸ Pharmacokinetic studies showed that clarithromycin, in combination with its active 14-hydroxy metabolite, has a longer half-life and higher plasma level than erythromycin, thus allowing twice-a-day dosing.³⁹ It is concentrated in cells and tissues, including tonsil, nasal mucosa, middle ear fluid and lung. Higher concentrations of drug are achieved in lung tissue than in concurrent samples of plasma.^{38,40} Appears to be safe and generally very well tolerated. In comparative clinical trials, overall adverse event rates associated with clarithromycin were similar to those with amoxicillin, penicillin, cefaclor and cefadroxil.³⁸ Related gastrointestinal side effects were shown to

occur at a lower frequency than those associated with erythromycin.⁴¹ Clinical efficacy has been demonstrated in randomized trials of children with acute otitis media, streptococcal pharyngitis, infections of skin and skin structures, and some lower respiratory infections or diseases such as bronchiolitis or pneumonia.^{38,42,43}

Considering the evidence described above, the objective of this systematic review with meta-analysis was to evaluate the efficacy and safety of clarithromycin in pediatric patients with upper respiratory infections.

METHODOLOGICAL DESIGN OF THE REVISION

Criteria used for study inclusion in this review

- **Types of studies.** We selected all of the published RCTs that compared, as some of its treatment branches, clarithromycin *vs.* another antibiotic in children with URIs who were ≤ 12 years.
- **Types of participants.** We selected for our review the articles that included children ≤ 12 years of age who had any upper respiratory tract infection (acute pharyngitis, tonsillitis, pharyngo-tonsillitis, bacterial acute rhinitis, or acute otitis media).
- **Types of interventions.** All of the RCTs that evaluated the efficacy and safety of clarithromycin compared with other antibiotics in children ≤ 12 years with URIs were included in the study (regardless of dose, route of administration, and duration of treatment).
- **Types of outcomes analyzed.** The outcomes analyzed were:
 - Bacteriological eradication.
 - Clinical cure [defined as complete resolution of clinical signs and symptoms, and documentation of a nonhyperemic, nonbulging tympanic membrane with effusion (flattened tympanogram) or without effusion (normal tympanogram)].
 - Clinical success (defined as cure plus improvement).
 - Relapsing rate (defined as the return of pre-treatment signs and symptoms of infection within 4 days after completion of treatment), and
 - The presence of any related adverse events.

Search methods for the identification of studies

Two authors of this review conducted simultaneous and independent searches of the literature on this topic, both in English and Spanish. The databases used included The Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library (Issue 5, 2010); MEDLINE (1966-January 2010), using the highly sensitive search strategy developed by The Cochrane Collaboration for the identification of RCTs;⁴⁴ and EMBASE (1980 to May 2010), using the search strategy adapted by the Cochrane Collaboration to search for RCTs in this database.⁴⁵ Additionally, we searched for further information in Lilacs (from 1980 to 2011), Artemisa (from 1999 to 2009) and in the gray literature that was obtained through a manual search or a query via email.

Information collection and analysis

- **Selection of studies.** The evidence review was conducted blindly and independently by three of the authors of this review. These authors, after carefully analyzing each item, excluded the studies that were considered irrelevant for the purposes of this review. If there were any discrepancies between the reviewers, an agreement was reached through the Delphi panel method.
- **Information extraction.** Information extraction was performed using forms of standardized data extraction including:
 - Title of the article.
 - Test design.
 - Method of randomization.
 - Type of blinding.
 - Presence of intention to treat analysis.
 - Allocation scheme.
 - Total number of participants.
 - Detailed explanation of follow-up failures.
 - Stages of completion of the study (multicenter or single center).
 - A description of the population.
 - A detailed description of maneuvers, and
 - A detailed description of the outcomes.

When appropriate, the subgroups were also described based on:

- Duration of follow-up by subgroups, and
- Description of the presence of risk factors.

- **Classification of allocation schemes.** Allocation schemes were classified as adequate (methods of randomization that allow neither the researcher nor the participant to know or influence the allocation of patients), unclear (insufficient information to make judgments) or inadequate (description of randomization methods, such as non-opaque envelopes or the presence of information that would allow a biased assignment of the subject to a specific group).
- **Classification of the types of blinding.** These were classified according to the blinding of the investigator, the participant or the assessor in regards to the outcome and what was appropriate in terms of the objective (open, single, double or triple blinding).
- **Classification of the intention to treat analysis (ITA).** The ITA was classified as either clearly described, not described but confirmed on the study assessment or absent.

Statistical analysis

Statistical analysis was conducted using the STATA statistical package 11.0 for Mac considering the subroutines for the development of the meta-analysis. For dichotomous outcomes (e.g., bacteriological eradication *vs.* no eradication), the results were expressed as a risk ratio (RR) with confidence intervals at 95% (CI 95%). For continuous measurements, data were expressed as a weighted mean difference (WMD). In those cases for which the primary survey identified a value of heterogeneity (I^2) above 60%, the results were analyzed using a random effects model (inverse variance). Statistical heterogeneity was explored using Egger graphs, and the publication bias was evaluated using funnel plots.

RESULTS

We originally identified a total of 76 controlled clinical trials that were reviewed in their entirety, resulting in the rejection of 52 articles; thus, a total of 24 articles were selected for development of evidence tables and the meta-analysis⁴⁵⁻⁶⁹ (Tables 1-2). Clarithromycin was therapeutically equivalent to other antibiotics studied with respect to clinical cure

Table 1. Characteristic of included studies.

Author, year	Type of study*	Disease**	Age	n1	n2	Clarithromycin doses	Antibiotic control doses
Still, 1993	RSBCT-Published	FAA	6 m-12 y	176	191	Clarithro 7.5 mg/kg/bid/5-10d	Penicillin V 13 mg/kg/tid/10d
Bedregal, 1995	RSBCT-Published	FAA	2 y-15 y	22	21	Clarithro 15 mg/kg/bid/5-10d	Penicillin V 13 mg/kg/tid/10d
Padilla-Raygoza, 1995	RSBCT-Published	FAA	1 y-12 y	102	99	Clarithro 15 mg/kg/bid/10d	Amoxycillin-Clavul 40 mg/kg/tid/10d
Padilla, 1996	ROBCT-Poster	FAA	1 y-16 y	102	99	Clarithro 7.5 mg/kg/bid/5-10d	Amoxycillin-Clavul 13 mg/kg/tid/10d
Castarño, 1996	ROBCT-Poster	FAA	3 y-15 y	34	37	Clarithro 7.5 mg/kg/bid/5-10d	Cefadroxil 15 mg/kg/vida/10d
Kearsley, 1997	RSBCT-Published	FAA	1 y-12 y	98	91	Clarithro 7.5 mg/kg/bid/5-10d	Amoxycillin 10 mg/kg/tid/5-10d
Venuta, 1998	RDBCT-Published	FAA	6 m-12 y	74	63	Clarithro 7.5 mg/kg/bid/5-10d	Azitromicin 10 mg/kg/tid/10d
McCarthy, 2000	RDBCT-Published	FAA	6 m-12 y	288	260	Clarithro 7.5 mg/kg/bid/5-10d	Penicillin V 13 mg/kg/tid/10d
Oliveros-Lozano, 2001	ROBCT-Published	FAA	2 y-12 y	87	102	Clarithro 7.5 mg/kg/bid/5-10d	Amoxycillin 50 mg/kg/bid/5-10d
Kafetziz, 2004	ROBCT-Published	FAA	3 y-13 y	86	88	Clarithro 7.5 mg/kg/bid/5-10d	Cefprozil 30 mg/kg/bid/5d
Syrogianopoulos, 2004	ROBCT-Published	FAA	2 y-16 y	155	155	Clarithro 15 mg/kg/bid/5d	Amoxycillin-Clavul 44 mg/kg/tid/5d
Padilla-Raygoza, 2005	RSBCT-Published	OMA	1 y-17 y	91	91	Clarithro 15 mg/kg/bid/5-10d	Azitromicin 10 mg/kg/tid/5-10d
Coles, 1993	RSBCT-Published	OMA	1 y-12 y	132	127	Clarithro 7.5 mg/kg/bid/5-10d	Amoxycillin 10 mg/kg/tid/5-10d
Gooch, 1993	RSBCT-Published	OMA	6 m-12 y	150	131	Clarithro 7.5 mg/kg/bid/5-10d	Cefador 20 mg/kg/bid/5-10d
Pukander, 1993	RSBCT-Published	OMA	1 y-12 y	39	40	Clarithro 7.5 mg/kg/bid/5-10d	Amoxycillin 20 mg/kg/tid/5-10d
McCarthy, 1993	RSBCT-Published	OMA	6 m-12 y	161	177	Clarithro 7.5 mg/kg/bid/10d	Amoxycillin-Clavul 13 mg/kg/tid/10d
Aspin, 1994	ROBCT-Published	OMA	6 m-12 y	90	90	Clarithro 15 mg/kg/bid/10d	Amoxycillin-Clavul 40 mg/kg/tid/10d
Ramet, 1994	ROBCT-Published	OMA	5 m-6 y	72	75	Clarithro 7.5 mg/kg/bid/5-10d	Azitromicin 10 mg/kg/tid/5-10d
Arguedas, 1995	ROBCT-Poster	OMA	9 m-11 y	45	48	Clarithro 7.5 mg/kg/bid/5-10d	Azitromicin 10 mg/kg/tid/5-10d
Ramet, 1996	ROBCT-Poster	OMA	5 m-7 y	102	97	Clarithro 7.5 mg/kg/bid/5-10d	Amoxycillin-Clavul 7-10 mg/kg/tid/10d
Craft, 1996	ROBCT-Poster	OMA	1 y-12 y	22	24	Clarithro 7.5 mg/kg/bid/5-10d	Amoxycillin 14 mg/kg/tid/5-10d
Kafetziz, 1996	ROBCT-Poster	OMA	6 m-52 m	15	15	Clarithro 7.5 mg/kg/bid/5-10d	CefuroximeAxetil 15 mg/kg/bid/5d
Syrropoulou, 1996	ROBCT-Poster	OMA	5 m-12 y	38	31	Clarithro 7.5 mg/kg/bid/5-10d	Cefaclor 13 mg/kg/tid/10d
Gooch, 1999	RSBCT-Published	OMA	6 m-3 y	117	117	Clarithro 7.5 mg/kg/bid/10d	Loracarbef 15 mg/kg/bid/10d

*RDBCT: randomized double blind controlled trial. RSBCT: randomized single blind controlled trial. ROBCT: randomized open blinded controlled trial. ** FAA: acute pharyngitis. OMA: acute otitis media.

Table 2. Characteristic of included studies (continued).

Author, year	Clinical cure Clarithro (%)	Clinical cure Control (%)	Clinical success Clarithro (%)	Clinical success Control (%)	Bacterial cure Clarithro (%)	Bacterial cure Control (%)	Adverse events Clarithro (%)	Adverse events Control (%)
Still, 1993	NR*	NR	0.96	0.94	0.95	0.85	0.20	0.06
Bedregal, 1995	0.86	0.90	NR	NR	0.86	0.90	NR	NR
Padilla-Raygoza, 1995	NR	NR	0.93	0.87	0.87	0.81	0.02	0.12
Padilla, 1996	NR	NR	0.94	0.86	0.88	0.86	NR	NR
Castafío, 1996	0.94	0.95	NR	NR	0.91	0.92	NR	NR
Kearsley, 1997	NR	NR	0.99	0.99	NR	NR	NR	NR
Venuta, 1998	0.96	0.97	NR	NR	0.81	0.94	NR	NR
McCarty, 2000	NR	NR	0.97	0.94	0.94	0.78	NR	NR
Oliveros-Lozano, 2001	0.95	0.96	NR	NR	NR	NR	NR	NR
Kafetziz, 2004	0.98	0.99	NR	NR	0.73	0.92	0.06	0.05
Syrogianopoulos, 2004	NR	NR	0.80	0.85	0.48	0.51	0.14	0.15
Padilla-Raygoza, 2005	NR	NR	0.90	0.89	0.95	0.79	NR	NR
Coles, 1993	0.69	0.56	0.83	0.80	NR	NR	0.03	0.06
Gooch, 1993	NR	NR	0.86	0.90	NR	NR	0.20	0.24
Pukander, 1993	0.92	0.90	NR	NR	NR	NR	0.26	0.18
McCarty, 1993	NR	NR	0.75	0.75	NR	NR	0.12	0.32
Aspin, 1994	0.89	0.91	NR	0.00	NR	NR	0.18	0.48
Ramet, 1994	NR	NR	0.99	0.99	NR	NR	0.14	0.15
Arguedas, 1995	NR	NR	0.96	0.98	NR	NR	NR	NR
Ramet, 1996	0.90	0.93	NR	NR	0.92	0.95	NR	NR
Craft, 1996	0.91	0.79	0.95	0.92	0.50	0.33	NR	NR
Kafetziz, 1996	0.87	0.87	0.87	0.87	NR	NR	NR	NR
Syriopoulou, 1996	0.84	0.84	0.89	0.87	NR	0.00	NR	NR
Gooch, 1999	0.58	0.56	NR	NR	NR	0.00	0.41	0.46

*Non reported.

[RR 1.02 (0.98 to 1.06), p NS], clinical success [RR 1.01 (0.99 to 1.03), p NS] and relapse risk [RR 1.34 (0.81 to 2.21), p NS], but was associated with a better bacteriological eradication [RR 1.06 (1.02 to 1.09), p 0.001], and a lower risk for related adverse events [RR 0.77 (0.65 to 0.90), p = 0.001] (Figures 1-5).

DISCUSSION AND CONCLUSIONS

Since 1990, various clinical trials had been showed that clarithromycin is as effective as other antibiotics for the treatment of pediatric patients with URIs.⁴⁶⁻⁵⁹ In 1993, Coles, *et al.*, compared the safety and efficacy of clarithromycin and amoxicillin in the treatment of otitis media in pediatric patients. Two hundred and fifty-nine patients aged 1-12 were prescribed suspensions of clarithromycin (132 patients) or amoxicillin (127 patients). Both suspensions were prescribed at a dose of 125 mg for children weighing less than 25 kg or at 250 mg for children weighing more than 25 kg, but three doses of amoxicillin per day were given, while only two doses clarithromycin per day were required. Each

drug was administered for approximately 5 days. Clinical evaluations were performed pre-treatment (Study day 1), at the end of treatment (Study days 6-9), and post-treatment (Study days 28-32). At the end of treatment, 91 out of 114 evaluable patients (80%) had clinical cures with clarithromycin, while 71 out of 105 evaluable patients (68%) had clinical cures with amoxicillin (p = 0.057). Clinical success rates were 96% for both treatments (110/114, clarithromycin; 101/105 amoxicillin). Adverse events related to the study medications occurred in four of 132 patients receiving clarithromycin (3%) and eight out of 127 subjects receiving amoxicillin (6%). Three patients discontinued treatment due to adverse events, all three receiving amoxicillin. At the doses administered, clarithromycin given twice-daily was as safe and effective as given three-times-daily in the treatment of acute otitis media in pediatric patients.⁵⁷

In 1995, Ramet, *et al.*, evaluate safety and efficacy of short course treatment with a new oral suspension formulation of clarithromycin in 153 children aged 5 months to 6 years with signs and

symptoms of acute otitis media. Children were randomized to receive a 5-day course of clarithromycin oral suspension (7.5 mg/kg; maximum 500 mg) twice daily or azithromycin oral suspension (10 mg/kg on day 1, followed by 5 mg/kg daily for 4 days) once daily. Specific clinical response criteria were developed

based on pretreatment signs and symptoms. Of the 153 patients enrolled, 147 patients (96%) were evaluable (clarithromycin, 72; azithromycin, 75). There were no demographic differences between the two groups. Clarithromycin and azithromycin suspensions were similarly effective for the treatment of acute

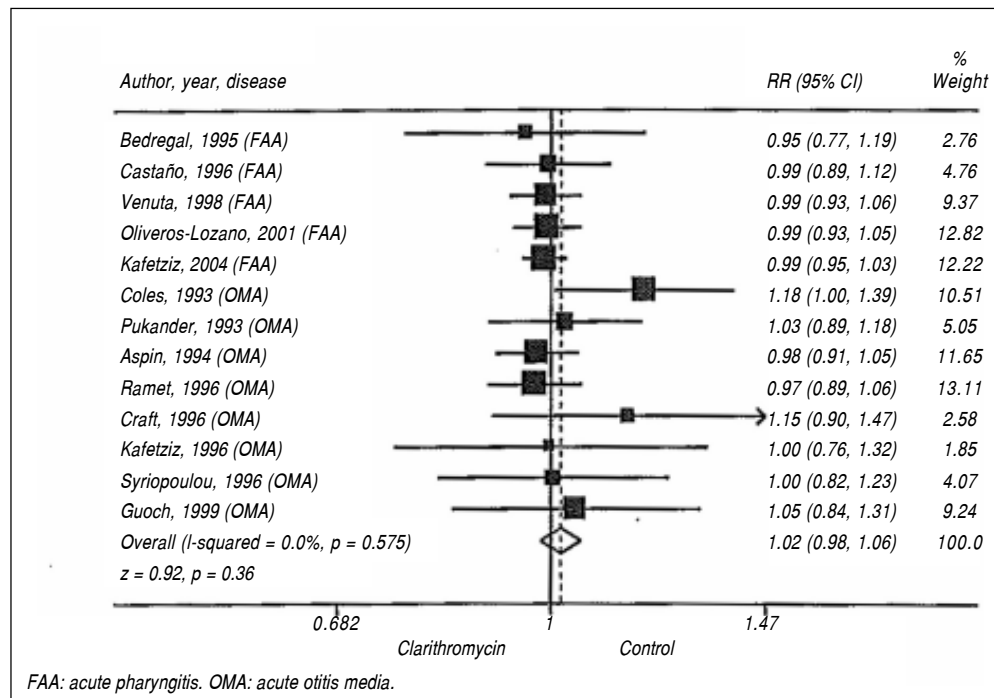


Figure 1. Efficacy of clarithromycin in pediatric patients with upper respiratory infections (clinical cure).

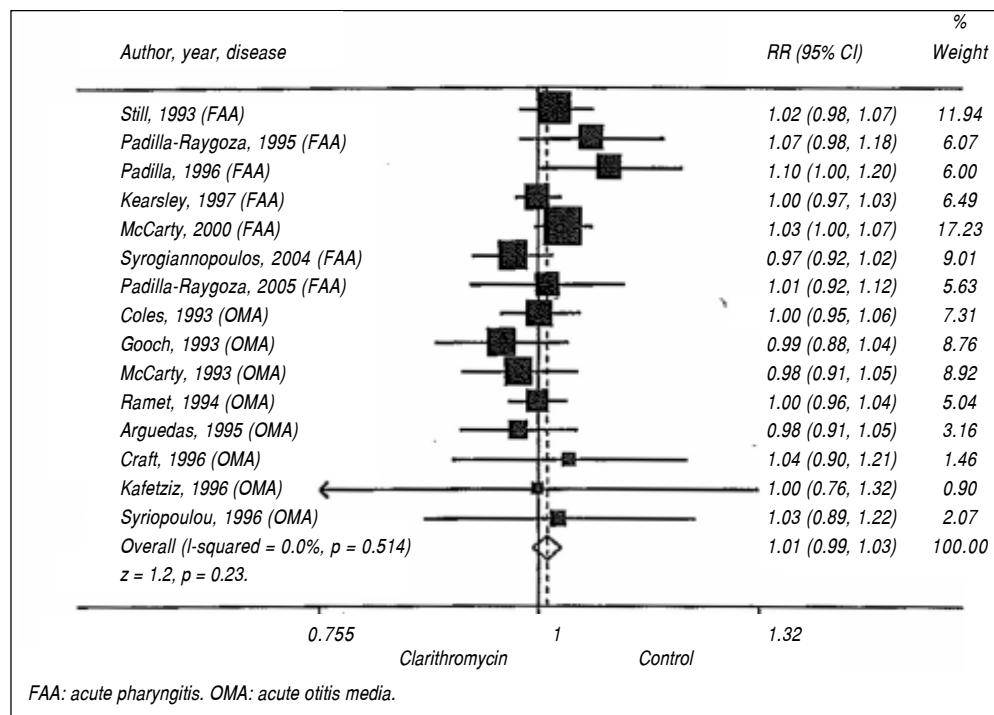


Figure 2. Efficacy of clarithromycin in pediatric patients with upper respiratory infections (clinical success).

otitis media. Clinical success (cure, cure with effusion, or improvement) was achieved in 99% of both clarithromycin- and azithromycin-treated patients. Both drugs were well tolerated; adverse events considered probably drug related were reported by 10 (13%) of clarithromycin recipients and 11 (14%) of

azithromycin recipients. There were no significant differences between the groups in the numbers of patients reporting events that were thought to be related to study medication. A 5-day regimen of clarithromycin suspension (7.5 mg/kg twice daily) appears to be as safe and effective as a 5-day regimen

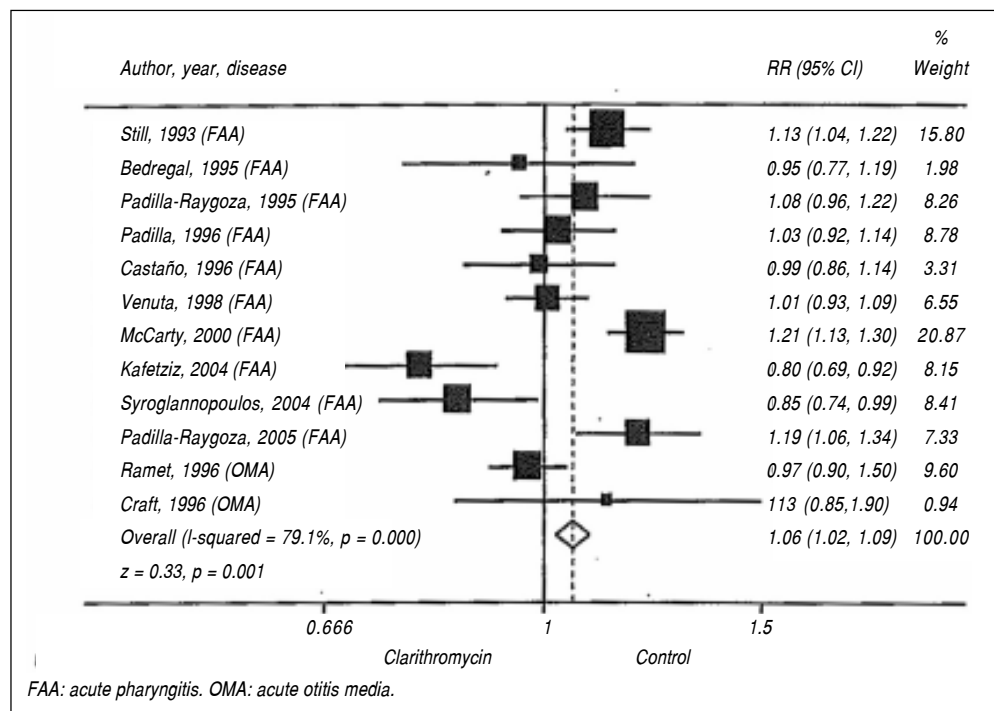


Figure 3. Efficacy of clarithromycin in pediatric patients with upper respiratory infections (bacteriological cure).

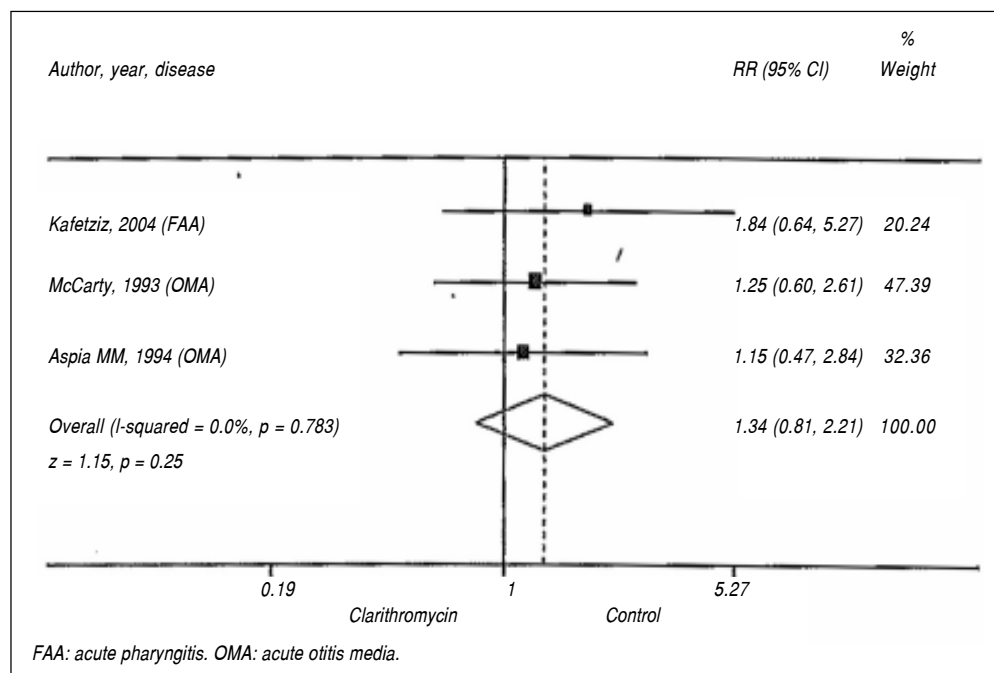


Figure 4. Efficacy of clarithromycin in pediatric patients with upper respiratory infections (relapse rate).

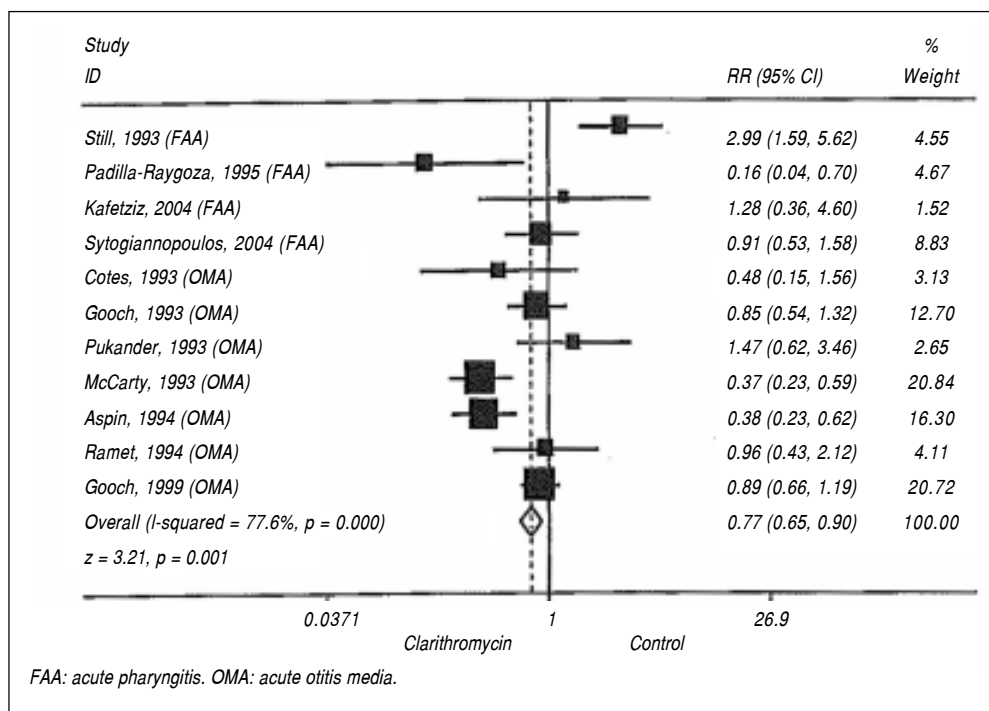


Figure 5. Safety of clarithromycin in pediatric patients with upper respiratory infections (adverse events risk).

of azithromycin suspension for the treatment of acute otitis media in children.⁶³

In 1997, Kearsley, *et al.*, compare in 229 paediatric patients (aged 1-12 years, body weight > 8 kg) with clinical evidence suggestive of streptococcal tonsillitis and/or pharyngitis clarithromycin suspension (7.5 mg/kg twice daily) or amoxicillin syrup (125 mg/kg three times daily body weight < 25 kg, or 250 mg/kg three times daily body weight 25 kg) for 7 days and were followed up 3-8 days post treatment and 21-28 days later. Clinical and microbiological assessments were made at each visit. A total of 189 patients (98 on clarithromycin and 91 on amoxicillin) were clinically evaluable. At the post-treatment visit, clinical success rates were high and comparable: 98% on clarithromycin and 97% on amoxicillin. *Streptococcus pyogenes* was eradicated in 88% of clarithromycin patients and 86% of amoxicillin patients. Both treatments were well tolerated. In conclusion, clarithromycin suspension was as safe and at least as effective as amoxicillin syrup for the treatment of pharyngitis and/or tonsillitis in children, and would be a suitable alternative therapy.⁵¹

Similar to previous published evidence, results of this systematic review with meta-analysis showed that clarithromycin was therapeutically equivalent to other antibiotics studied with respect to clinical cure, clinical success and relapse risk, but associa-

ted with a better bacteriological eradication and a lower risk for related adverse events. This data let consider that clarithromycin is a safe and effective alternative for the treatment of URIs in pediatric patients, being superior to other antibiotics in relation to bacterial eradication. Its equivalence profile related to clinical cure, clinical success and relapse risk, let to consider it as an important alternative for the treatment of children with upper respiratory infections, such as acute pharyngitis or acute otitis media.

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