

AZITHROMYCIN VERSUS CO-AMOXICLAV IN THE TREATMENT OF ACUTE SUPPURATIVE OTITIS MEDIA

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ABSTRACT

Objective: To compare the use of Azithromycin and co-Amoxiclav in the treatment of symptoms and signs of acute suppurative otitis media in children.

Methods: Children of four months to 12 years of age, attended out-patient Pediatric and ENT clinics at Princess Haya Al-Hussein Hospital in Aqaba from June 2003 to June 2004; with signs and symptoms of acute suppurative otitis media were enrolled in the study. Patients were randomized to receive either Azithromycin 10 mg/kg/day in a single dose for 3 days or co-Amoxiclav 45mg/kg/day in three divided doses for 10 days. Clinical improvement was evaluated on the 2nd and 4th weeks after therapy.

Results: Satisfactory clinical response was measured regarding symptoms and signs two weeks after the beginning of therapy. They were 84.6% for Azithromycin and 88% for Co-Amoxiclav. At day 28, 61 patients (82.4%) were cured on Azithromycin compared with 66 patients (83.5 %) on Co-Amoxiclav.

Conclusion: Azithromycin given for three days and Co-Amoxiclav for ten days had similar efficacy; however, Azithromycin was better tolerated.

Key words: Acute Suppurative Otitis Media, Children, Antibiotics.

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Introduction

Otitis Media is an inflammation in the middle ear. Subcategories include acute otitis media, otitis media with effusion (also known as “glue ear”), recurrent acute otitis media, and chronic suppurative otitis media. Acute otitis media presents with systemic and local signs and has a rapid onset. The persistence of an effusion beyond three months without signs of infection defines otitis media with effusion, whereas chronic suppurative otitis media is characterized by continuing inflammation in the middle ear giving rise to otorrhoea and a perforated tympanic membrane⁽¹⁾.

Our study is on Acute Suppurative Otitis Media (ASOM), which is a suppurative infection of the middle ear cavity and is most common in healthy children between 6 months and 2 years of age, it is more

common in boys, in patients of lower socioeconomic status, in formula fed infants, and in the winter months⁽²⁾. It is an important health problem in early childhood, and is the most frequent condition for which antibiotics are prescribed in the USA⁽³⁾.

The most common pathogens are streptococcus pneumonic Hemophilus Influenza, and Branhamella catarrhal, half of these organisms are β -lactamase producers. Very young children will not complain of pain but will be irritable and may bang the head on the cot sides. On examination, the young child is febrile restless and uncooperative with red bulging tympanic membrane. If the ears discharge, it is usually blood stained initially and this may worry parents. The discharge then became mucopurulent⁽⁴⁾.

A combination of important factors contributes to pathogenesis of ASOM. The most two important factors

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in children are Eustachian tube dysfunction and the child susceptibility to recurrent upper respiratory tract infections. In the child, the Eustachian tube is shorter (less distance for organisms to travel), placed horizontal (inadequate drainage of middle ear) and has adenoids present at the opening which can readily block the tube and serving as a reservoir of infection.

Bacteria are responsible for the majority of cases ⁽⁵⁾.

Antibiotic treatment of Acute Suppurative Otitis Media hastens symptomatic relief and potentially prevents the development of more serious invasive disease ⁽⁶⁾.

As there are a number of antibiotics used for this purpose we undertook this trial in children with ASOM to compare the use of two important antibiotics commonly used in this condition in Jordan.

Amoxicillin semi synthetic penicillin has broadened spectra against Gram-negatives and is effective orally. Amoxicillin plus Clavulanate is Clavamox or Augmentin. The Clavulanate is not an anti- microbial agent; it inhibits beta-lactamase enzymes and has given extended life to penicillinase ⁽⁷⁾. Generally ampicillin, amoxicillin, or co-Amoxiclav (amoxicillin-clavulanate) are preferred and most commonly used in ASOM in Jordan.

Azithromycin is an azolide antibiotic, it is active in vitro against a variety of microorganisms and has a greater distribution in tissues, a longer elimination half-life and a lower incidence of adverse effects than Erythromycin ⁽⁸⁾.

The purpose of this study was to compare the clinical use of Azithromycin with Amoxiclav.

Methods

This consecutive study was carried out at Princess Haya Hospital in Aqaba from June 2003 to June 2004, children attending outpatient ENT and pediatric OPD clinics. Children of ages four months to twelve years were enrolled in the study, if they satisfied one or more of the following criteria:

- Ear pain or fullness.
- Decreased hearing.
- Discharge from the external auditory canal.
- Bulging or marked injection of the tympanic membrane.
- Loss of the normal light reflex or tympanic membrane landmarks.
- As well as generalized symptoms; fever, general malaise, and irritability.

Exclusion criteria included: History of Macrolide or β -lactamase drug allergy, history of antibiotic treatment in the preceding four weeks, Symptoms persisting for more than four weeks, and children receiving antimicrobial prophylaxis.

Patients were randomized on alternative weeks and accordingly divided into two groups: First group

received either Azithromycin (10 mg/kg/day) once daily for three days, and second group were given Co-Amoxiclav (45mg/kg/day) in three divided doses for ten days.

Assessment of these patients was carried out on the initial visits and follow up was done on days 14 and 28.

Patients were identified to be: Cured when there were a complete resolution of all signs and symptoms, improved by partial resolution of signs and symptoms, and failed if there were no changes or worsening of symptoms signs.

On follow up visits complete Ear, Nose and Throat examination was performed by the same physicians at all pre treatment and post treatment visits.

Results

Two hundred three patients were initially enrolled in the study, 17 patients were non-eligible as 5 had allergy to Amoxicillin, and 12 didn't fulfill the inclusion criteria because they received antibiotics in the preceding four weeks.

Total number of patients found eligible in our study was 186 children all of these patients were randomized into two groups; first group included 91 children (received Azithromycin 10mg/kg/day once daily for three days), while the second group included 95 children and was given Co-Amoxiclav 45 mg/kg/day in three divided doses for 10 days). The mean age of patients enrolled was 3.4 years (range 4 months-12 years).

The most common symptom was ear pain (94%) while the most common sign was injection of tympanic membrane (93%). (Table I)

Patients post treatment evaluation was done at two weeks; in the first group, 66 out of 78 children (84.6%) showed improvement or were cured, compared to 74 out of 84 children (88%) in the second group.

However, at four weeks post treatment, 61 out 74 children (82.4%) in the first group were completely cured and did not need any further antibiotic treatment, compared again to 66 out of 69 children (83.5%) in the second group. (Table II, Fig. 1) Regarding the adverse effects to the drugs used these were mostly seen in children treated with Co-Amoxiclav compared with those who received Azithromycin and occurred in 18% and 10% respectively, the most commonly observed side effect with both drugs was diarrhea. Rash and vomiting were also seen.

Discussion

In Jordan, particularly the Royal Medical Services, Acute Suppurative Otitis Media is usually treated with antibiotics, and generally amoxicillin, or Co-Amoxiclav (amoxicillin-clavulanate) are preferred and this depends on the availability and the cost of these medications.

In his study, Dunne MW *et al* have provided evidence that Azithromycin for three days of treatment with a

total dose of 30mg/kg/day is as effective as Co-Amoxiclav given at 45mg/kg/day.

Similarly our study carried out on children of various age groups shown that the success rate of treatment at 2 and 4 weeks were nearly equivalent for both antibiotics and there was no significant difference (Table II).

Satisfactory clinical response regarding symptoms and signs evaluated at 2 weeks post treatment was 84.6% for Azithromycin and 88% for Co-Amoxiclav; this is compared to results seen in Dunne *et al* study where the clinical success (cure and improvement) in all subjects was 83% for Azithromycin group of patients, and was 88% for patients on Co-Amoxiclav on evaluation at 10 days post treatment.

However regarding Co- Amoxiclav, it was noted that it led to a quicker resolution of tympanic membrane signs such as bulging and loss of landmarks at two weeks after initiation of treatment, whereas at four weeks of treatment both agents showed a similar outcome.

As for the mechanism of action, Co-Amoxiclav is a bactericidal agent whereas Azithromycin is a protein synthesis inhibitor (bacteristatic) agent; it is an azolide antibiotic, which has a greater distribution in tissues, a longer elimination half-life, and a lower incidence of adverse effects than erythromycin. These

pharmacokinetic features allow once-daily dosing and a shorter duration of therapy^(9,10).

Our diagnoses were based on acute signs of infection and eardrum abnormalities, which is in keeping with the day-to-day practice in our hospital (The Royal Medical Services). There is a considerable controversy as to what antibiotic to use if at all, as some studies showed that up-to 80% of children with ASOM would resolve within one week without antibiotic treatment.

The generalized use of antibiotics in this condition increases health care costs and creates numerous side effects⁽¹⁰⁾. Watchful waiting at the first visit was justified by Damoiseaux *et al* for children aged 6-24 months with ASOM⁽¹¹⁾, and Froom *et al* state that Netherlands is the only country where only a minority of the episodes of Otitis Media is treated with antibiotics. The outcome of ASOM does not seem to be any worse than in other countries. In addition, as doctors are often uncertain about the diagnosis of Suppurative Otitis Media. Therefore, we recommend that clinicians should immediately reconsider the routine use of antimicrobials for children with Suppurative Otitis Media and consider treating symptoms with analgesics and observation for lack of improvement⁽¹²⁾.

In conclusion, azithromycin given for three days and co-Amoxiclav for 10 days had similar efficacy; however, Azithromycin was better tolerated.

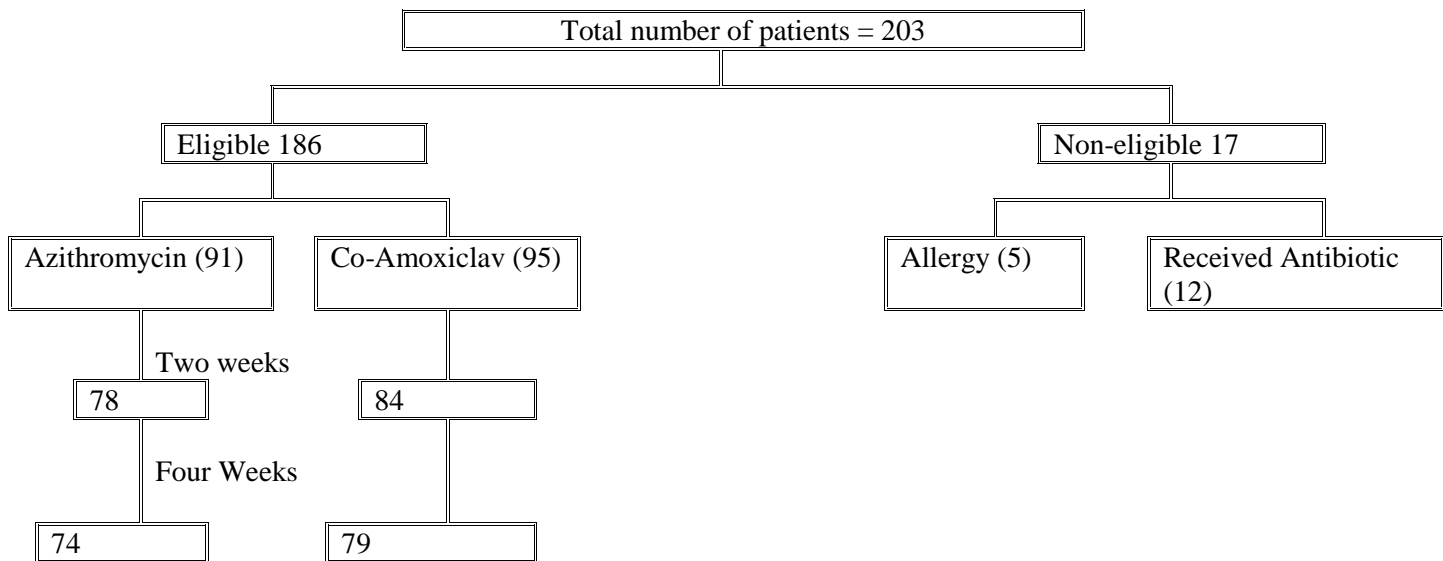


Fig. 1. Total number of patients

Table I. Signs and symptoms found at presentation.

Signs and symptoms	Number	%
Ear pain or fullness	175	94
Decrease hearing	23	12.3
Discharge from external auditory canal	13	7
Injection of tympanic membrane	172	93
Bulging of tympanic membrane	98	47.8
Perforated tympanic membrane	9	4.8
Generalized symptoms; fever, general malaise and irritability	69	37

Table II. Response after two and four weeks.

	Azithromycin	%	Co-Amoxiclav	%
Response at two weeks cured and/or improved	66/78	84.6	74/84	88
Response at four weeks cured and/or improved	61/74	82.4	66/79	83.5

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