INTRAMUSCULAR CEFTRIAXONE AS SINGLE DOSE TREATMENT OF ACUTE OTITIS MEDIA

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ABSTRACT

Objective: To evaluate single dose intramuscular ceftriaxone as an option for the treatment of acute otitis media (AOM). To compare efficacy of single dose intramuscular ceftriaxone to 10 days treatment with amoxicillin-clavulanate combination.

Design: Prospective, randomized, double blind control study.

Place and duration: Combined Military Hospital Muzaffarabad, Azad Kashmir, over a period of 02 years from October 2006 to September 2008.

Patients and methods: A total of 148 freshly diagnosed cases of AOM between ages 03months to 6 years were recruited and divided randomly into two equal groups of 74 each using random numbers table. Group I was administered oral amoxicillin-clavulanate in a dose of 45mg/kg/day in three divided doses along with single intramuscular shot of placebo. Group II was given a single shot of intramuscular ceftriaxone in a dose of 50mg/kg along with placebo syrup thrice a day for 10 days. Patients were reassessed at day 03 and 11.

Results: Ninety four point five percent of patients responded to amoxicillin-clavulanate whereas 95.9% responded to single dose IM ceftriaxone. No significant difference was noted between the two types of treatments in term of disease outcome.

Conclusion: Single dose intramuscular ceftriaxone can be another option for the treatment of AOM especially in children/parents with poor compliance.

Keywords: Acute otitis media in children, poor compliance, single dose intramuscular ceftriaxone,

INTRODUCTION

Acute otitis media (AOM) is one of the most common bacterial infections of early childhood for which antibiotics are prescribed[1,2]. Children experience an average of 1.5 episodes in the first year and spend approximately 2.5 months with middle-ear effusions related to AOM[3]. The most common pathogens that have been implicated are *Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis*[4,5]. Although the condition is said to be self resolving, antibiotics are prescribed to prevent serious complications such as acute mastoiditis, meningitis or facial paralysis[6]. Antibiotics not only relieve the symptoms quickly but also reduce the chances of hearing loss, permanent damage to the middle ear cleft and likelihood of complications[7]. Amoxicillin, amoxicillin-clavulanate (amoxi-clav), trimethoprim-sulfamethoxazole and erythromycin for a period of 10 days are the most frequently prescribed oral antibiotics for the treatment of AOM. However adherence to thrice a day dosage schedule when administering oral antibiotics to treat pediatric patients is problematic for both patients and parents. Children often feel difficulty in swallowing or may vomit or spit up the medication. Moreover administration of multiple daily doses to children can be especially inconvenient for working parents. Poor compliance to continue with the full course of treatment has raised concerns about emergence of resistant strains of bacteria and persistence of middle ear symptoms[8]. Alternative therapies have included ceftriaxone, a third-generation cephalosporin with a spectrum of antibacterial activity that includes most of the common pathogens of acute otitis media. It has been claimed that a single intramuscular shot of ceftriaxone is effective in the treatment of AOM.

The goal of this study was to compare the effectiveness of a single intramuscular dose of ceftriaxone with a 10-day course of oral amoxi-

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Received: 24 Jan 2011; Accepted: 29 Aug 2012

clav treatment in infants and children with AOM.

MATERIALS AND METHODS

These double blinded randomized controlled trials were carried out at Combined Military Hospital Muzaffarabad, Azad Kashmir over a period of 02 years from October 2006 to September 2008.

A total of 1480 freshly diagnosed cases of acute AOM between the ages of 03 months to 06 years were recruited into the study. Only uncomplicated cases were included.

Patients who have already received any antibiotic treatment for any reason within the past two weeks were excluded. All cases that had undergone suppuration were not included.

AOM occurring in children who were known cases of otitis media with effusion (whether under observation or undergone myringotomy and ventilation tube placement) were excluded from the study. Patients who did not report for follow ups or who did not also comply with a complete 10 day treatment were excluded from the study. Patients who needed any other treatment for any other associated illness were excluded. Children with other underlying diseases that impair response to treatment like cleft palate, Down's syndrome and immunodeficiency states were also excluded.

Diagnosis was based upon history and clinical findings of otoscopy. Patients were randomly divided into two equal groups of 74 each using random numbers table. Group I was given a 10-day treatment of orally administered amoxicillin and clavulanate (45 mg/kg/ day) divided into 3 doses along with a single intramuscular shot of placebo. Group II patients received a single dose of ceftriaxone (50 mg/kg, not exceeding 1 g) and oral placebo syrup 08 hourly for a period of 10 days in a double blind fashion. Informed consent was obtained from aal parents. Parents of both patient groups were instructed both verbally and in writing to administer the medication 3 times daily for 10 days. In addition all patients received adequate analgesics and antipyretics. Patients were requested to bring their remaining study medicine along at every visit during the 10 day course. Patients were re-assessed at day 03 and day 11. The symptoms and otoscopic findings were evaluated and recorded according to a scoring system (table 1). Decreasing score at subsequent visit was taken as improvement whereas same or increasing score was taken as treatment failure. All data was recorded on a standardized form, later shifted to SPSS version 10.0 and analyzed. Descriptive statistics were used to describe the data. Chi square test was applied to compare qualitative variables between the two groups and a p value < 0.05 was considered to be statistically significant.

RESULTS

A total of 148 patients were recruited into the study and divided into two equal groups of 74 each. There were 37 males in group I and 41 males in group II. According to age distribution and gender, no significant difference was determined among the groups ($p>0.05$). The progression of disease with the two drug regimes have been shown in figures 1-2. In group I, 70/74 (94%) patients responded satisfactorily to amoxicillin-clavulanate combination where as in group II, 71/74 (96%) patients responded. It was noted that there was no significant difference between the two types of treatments in terms of disease outcome (p = 1.000). None of the possible complications (temporal or intracranial) of AOM were seen in either patient group. Moreover no significant complications to any of the antibiotics were seen which would have necessitated a discontinuation and/or change of medication.

DISCUSSION

The choice of antibiotic for the treatment of AOM has been a matter of debate for quite some time. The increasing resistance rate of pneumococci to penicillin and emergence of beta-lactamase-producing *H. influenzae* and *M. catarrhalis* raises difficulties in the choice of appropriate therapy[9]. Because of its low cost and relative safety, amoxicillin is still considered first-line therapy for AOM; however, it doesn't cover beta-lactamase-producing *H. influenzae* and *M. catarrhalis*. For the presence of beta lactamase-producing pathogens, clavulanic acid has been added to

amoxicillin. Ceftriaxone, a third generation cephalosporin has been reserved for patients of AOM failing oral therapy or those with severe disease[10,11]. Though it is not the first line treatment for AOM, it is of great use in regions where penicillin resistance is believed to be high and in persistent infections presumed to be secondary to resistant organisms. Ceftriaxone has a good antibacterial activity against most pathogens causing AOM and reaches 10% of its serum concentration in the middle-ear fluid. This concentration in middle ear exceeds the minimum inhibitory concentrations (MIC) of the typical AOM pathogens for approximately 56 hours after a single intramuscular injection of 50 mg/kg[12]

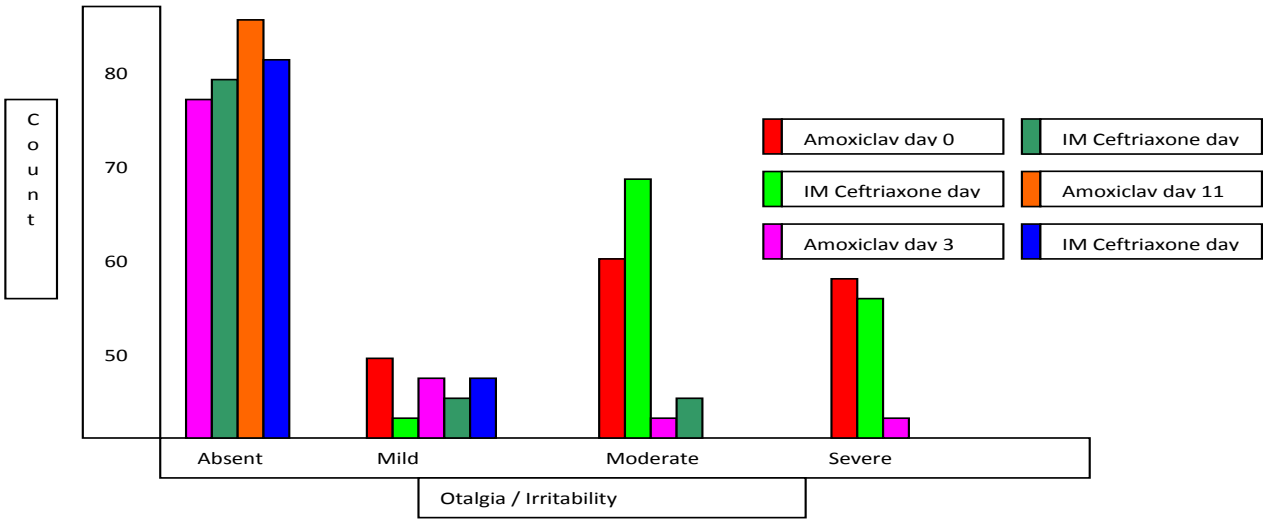

Fig. 1: Progressively decreasing Otalgia with Treatment comparison between the two drug regimes.

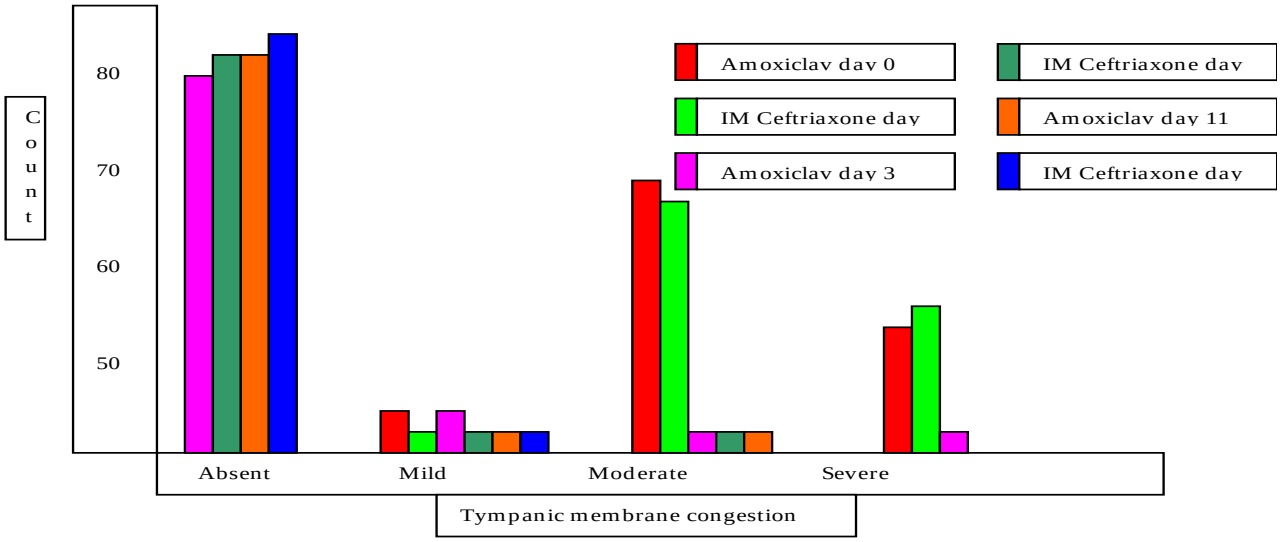

Fig. 2: Progressively decreasing tympanic membrane congestion with treatment comparison between the two drug regimes.

Table: Clinical scoring system.

Symptoms (Otalgia/ Irritability)		**Otoscopy (Erythema/ congestion)**	
Absent	0	Absent	0
Mild	1	Mild	1
moderate	2	moderate	2
Severe	3	Severe	3

which makes a single shot of IM ceftriaxone sufficient for the treatment of uncomplicated AOM. Single shot IM ceftriaxone has a huge advantage over prolonged regimes in children who might refuse to take or vomit oral medications and for families who might have compliance problems. For the same reasons Bauchner had demonstrated significant preference of parents for intramuscular ceftriaxone over 10 days course of oral antibiotic[13]. Although a single injection of intramuscular ceftriaxone is approved for the treatment of AOM, it is recommended as daily injections on three consecutive days for patients in whom initial therapy with high-dose amoxicillin (± clavulanic acid) is unsuccessful[14].

The results of our study have shown that there is no significant difference among the two regimes in terms of treatment outcome clinically (p=1.000). Ninety four point five percent of the cases responded to amoxi-clav combination where as 95.9 % of cases responded to single IM dose of ceftriaxone. Similar results have been reported by Wang[15], Varsano[16], Zhang[17], Biner[18,19] and many others. This shows that treatment with single IM injection of ceftriaxone in the dose of 50mg/kg body weight is as effective as 10 days course of oral amoxicillin-clavulanate combination.

A great point of concern with such single dose regimens has been the fear of emergence of resistant strains which might make a very safe, third generation, life saving, cephalosporin relatively ineffective in more dire circumstances. Few of the authors have claimed that use of single dose ceftriaxone resulted in significant changes in the nasopharyngeal bacterial flora thereby increasing the prevalence of pneumococcal strains which have decreased sensitivity to penicillins[20]. On the other hand others claim that though there may be a chance of emergence of penicillin resistant pneumococci, there are no significantly increased chances of emergence of penicillin resistant *S. pneumoniae*[21], nor there was any change in the prevalence of antibiotic-resistant gram-negative facultative bacilli in the stool of healthy children when compared with commonly used oral agents[22]. Others have suggested that single dose intramuscular ceftriaxone resulted in significant reductions in the nasopharyngeal colonization rates with all three major AOM pathogens[23]. Probably the only disadvantages of ceftriaxone include the discomfort of an injection to young children and a greater overall cost[24]. We must also keep in our mind the fact that most of the "thrice-a-day for 10 days" regimens are also not being followed religiously because of the many parent and patient factors and that too is resulting in emergence of penicillin resistant strains.

CONCLUSION AND RECOMMENDATIONS

Single dose intramuscular ceftriaxone is as effective as 10 days oral amoxicillin clavulanate combination for the treatment of acute otitis media in children. However because of fear of emergence of resistant strains this should be reserved only for the patients and parents with questionable compliance (e.g. when the ability to tolerate or absorb oral drugs is compromised, irritable behavior, refusal to take drug, schooling and job compulsion of parents).

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