Articolo originale

Original article

Comparison of cefuroxime and co-amoxiclav in the treatment of acute sinusitis in a sample of the Iranian population

Confronto tra cefuroxime e co-amoxiclav per il trattamento della sinusite acuta in una popolazione di pazienti in Iran

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INTRODUCTION

Acute sinusitis is a common upper respiratory tract infection worldwide. The presenting signs and symptoms of acute sinusitis include fever, headache, facial pain, nasal congestion, cough, and purulent nasal discharge. Symptoms lasting less than four weeks define an acute episode of sinusitis, whereas symptoms of chronic sinusitis persist longer [1, 2].

Bacterial sinus infections are common, either as a primary cause of acute sinusitis or as secondary complications of upper respiratory viral infections or allergic rhinitis [1, 2]. Acute sinusitis is usually diagnosed and treated in general clinical practice. Since the presenting signs and symptoms of acute bacterial sinusitis can be indistinguishable from those of a viral upper respiratory tract infection or allergy, use of antibiotics is advised.

A recent meta-analysis of the results of randomized clinical trials comparing the efficacy of antibiotics versus placebo in acute sinusitis [1, 3] found that antibiotics were more effective in achieving a clinical cure than placebo. However, this analysis also concluded that antibiotics were generally more effective when stringent criteria (including sinus aspiration for identification of pathogens and/or sinus radiography) were used to diagnose acute sinusitis. It is often impractical in general practice to obtain bacteriologic confirmation of the causative pathogen, and empiric antibiotic treatment is typically prescribed for acute bacterial sinusitis. Empiric antibiotic therapy should provide coverage against the most common pathogens identified in acute bacterial sinusitis including *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* [4].

Almost 100% of *M. catarrhalis* isolates and up to 40% of *H. influenzae* strains produce beta-lactamase and may show decreased susceptibility to some beta-lactam antibiotics [5, 6]. Atypical organisms such as *Chlamydia pneumoniae* and *Legionella pneumophila* are uncommon causes of acute sinusitis [1, 7].

Therefore, broad-spectrum antibiotics with activity against beta-lactamase-producing pathogens are necessary for effective management of acute bacterial sinusitis [1, 7].

Cefuroxime is an oral second generation cephalosporins characterized by a high degree of sinus tissue penetration and stability to beta-lactamases [8].

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It demonstrates *in vitro* activity against a wide range of gram-positive and gram-negative organisms (beta-lactamase producing and non beta-lactamase producing), including the bacterial pathogens commonly associated with acute sinusitis [9, 10]. The combination of amoxicillin with the beta-lactamase inhibitor clavulanate potassium is similarly active *in vitro* against both beta-lactamase-producing and non-beta-lactamase producing strains of common respiratory pathogens.

Both cefuroxime and co-amoxiclav are antimicrobial of choice in the treatment of acute bacterial sinusitis.

The purpose of the present study was to compare the efficacy of 10-day courses of cefuroxime 250 mg twice daily and co-amoxiclav 500/125 mg three times daily in patients with acute bacterial sinusitis in a sample of Iranian population.

PATIENTS AND METHODS

This was a randomized single-blind study conducted using a systematic random sampling technique at two outpatient clinics affiliated with Iran University of Medical Sciences, Tehran, Iran in 2007.

All patients provided written informed consent before entering the study.

Ninety-nine patients aged 12 years and older presenting with a clinical diagnosis of acute sinusitis and an initial onset of symptoms within the previous 30 days were recruited for the study. Eligible patients were required to have ≥2 of the following symptoms: rhinorrhea, nasal congestion, or cough.

In addition, radiographic evidence of opacification, 24-mm membrane thickening, and/or air-fluid level in one or both maxillary sinuses was required.

Other clinical symptoms that were assessed but were not essential for enrollment included fever, facial pain, postnasal drip, headache, sore throat, toothache, earache, malaise, and sinus fullness.

Patients were excluded if they had a diagnosis or history of chronic sinusitis; required sinus surgery or had undergone sinus washout in the previous seven days or sinus surgery in the past month; had received treatment with systemic antibiotics in the previous seven days; needed to initiate steroid therapy or to increase the dose of existing steroid therapy during the study; had known hypersensitivity to penicillin, cephalosporins, or beta-lactam antibiotics; had moderate or severe hepatic or renal impairment; had known neutropenia; had a history of a gastrointestinal disorder that could diminish antibiotic absorption; were immunocompromised; or had participated in a clinical trial within one month of enrollment. Pregnant or lactating women were also excluded.

Patients were randomized to receive either cefuroxime (250 mg BID) (n=57) or co-amoxiclav (500/125 mg TID) (n=42) for 10 days.

Patients were assessed during treatment (6 to 8 days after the start of treatment) and post-treatment (2 to 5 days after cessation of treatment). At each visit, the investigator assessed whether the following signs and symptoms were absent: rhinorrhea, headache, toothache, nasal congestion, cough, sore throat, earache, sinus fullness, facial pain and/or tenderness, postnasal drip, malaise, and cervical lymphadenopathy.

The clinical response to treatment was classified as cure (clinical signs and symptoms significantly improved or resolved at 2 to 5 days post-treatment) and failure (no improvement in clinical signs and symptoms by the first post-treatment visit or discontinuation due to a drug-related adverse event).

Baseline demographic and other patient characteristics were compared using the ^{2} test, as were the clinical cure rates for cefuroxime and co-amoxiclav in clinically evaluable patients at post-treatment.

Clinically evaluable patients were those who met the inclusion criteria and had received the intended amount of study drug, had undergone the test-of-cure assessment, and had not received any other antibiotic during the study or before the test-of-cure visit for an infection other than sinusitis. The Statistical Package for the Social Sciences (SPSS) was used to conduct the analyses.

RESULTS

A total of 99 patients with acute sinusitis were enrolled; 57 received cefuroxime and 42 received co-amoxiclav.

Patients' demographic characteristics and their frequency of clinical symptoms at enrollment (Table 1) were comparable between the two study groups.

No statistically significant differences were found between the groups in terms of age, sex

Table 1 - Demographic characteristics and symptoms and signs of study patients with acute sinusitis

	Cefuroxime	*Amoxicillin/clavulanate*	*P-value*
Sex, no. (%)			P >0.05
Male	24 (42.1)	16 (38.1)	
Female	33 (57.9)	26 (61.9)	
Age (year)			
Mean ± SD	29.7 ± 12.5	28.9 ± 10.5	P >0.05
Range	10-59	11-50	
Nasal Discharge			P >0.05
Absent	37 (62.7)	26 (65.0)	
Present	22 (37.3)	14 (35.0)	
Post Nasal Drip (PND)			P >0.05
Absent	0 (0)	1 (2.5)	
Present	59 (100.0)	39 (97.5)	
Cough			P >0.05
Absent	6 (10.2)	5 (12.5)	
Present	53 (89.8)	35 (87.5)	
Sinus Pain			P >0.05
Absent	15 (25.4)	4 (10.0)	
Present	44 (74.6)	36 (90.0)	
Facial Swelling			P >0.05
Absent	52 (88.1)	34 (85.0)	
Present	7 (11.9)	6 (15.0)	
Toothache			P >0.05
Absent	51 (86.4)	32 (80.0)	
Present	8 (13.6)	8 (20.0)	
Headache			P >0.05
Absent	48 (81.4)	28 (70.0)	
Present	11 (18.6)	12 (30.0)	
Fever			P >0.05
Absent	30 (50.8)	14 (35.0)	
Present	29 (49.2)	26 (65.0)	

and clinical presentation distribution. A satisfactory clinical outcome (cure or improvement of symptoms) was found in 86% (49/57) and 71.4% (30/42) of the clinically evaluable patients treated with cefuroxime or co-amoxiclav, respectively (p >0.05).

DISCUSSION

Cefuroxime has been produced by Iranian pharmaceutical companies and introduced to the market. Prior to introducing cefuroxime in Iran, if a patient with acute sinusitis did not respond to the treatment with co-amoxiclav, clinicians usually considered a third generation cephalosporin as an alternative choice. This could have caused an emerging antibiotic resistant problem in the country. The findings of this study are extremely important in economically developing countries such as Iran given the fact that the efficacy of cefuroxime and co-amoxiclav were found to be comparable. It should also be noted that it may be more convenient to use cefuroxime twice daily than using co-amoxiclav three times a day.

In this study, the clinical cure and improvement rates for both treatment protocols were some-

what higher than other studies [1, 6, 11]. This may be related to the fact that in addition to clinical signs/symptoms, sinus radiography was also considered in the criteria used in other studies to evaluate response rate. We believe that not including sinus radiography as a variable in our study may have caused higher cure rate compared to other studies. It should be noted that in patients with acute bacterial infections superimposed on a chronic sinus inflammation or membrane thickening (chronic sinusitis), the imaging may still show abnormalities after completion of the treatment. This can be interpreted as failure in treatment based on radiologic clearance. In fact, radiographic sinus abnormalities in the absence of clinical signs and symptoms of disease may indicate persistent inflammation or slow clearance of secretions rather than unresolved bacterial infection [1, 6, 11].

A recent meta-analysis determined that antimicrobial therapy was significantly more effective than placebo in acute sinusitis but that patients who benefited the most were those with clinical as well as radiographic evidence of sinusitis [3]. Typically, physicians include the patient's well-being and the resolution or improvement of symptoms over time in the clinical definition of successful therapy and follow-up radiography is not practical or advised in most primary care settings. The authors acknowledge this (lack of follow-up radiography) to be one of the limitations to this study.

Findings of this study support those of other clinical studies demonstrating comparable efficacy of cefuroxime compared with co-amoxiclav [1, 12-16]. This study provides further evidence that cefuroxime is an effective treatment for patients with acute sinusitis. The broad spectrum antibacterial activity of cefuroxime, including its excellent activity against the major causative bacterial pathogens in acute sinusitis and its high degree of stability to beta-lactamases, makes it an appropriate therapeutic option in the treatment of acute bacterial sinusitis. Further, the patient's compliance for cefuroxime is higher than that for co-amoxiclav since cefuroxime is prescribed twice daily compared to co-amoxiclav three times a day.

It is worth noting that cefuroxime is an old antibiotic in economically developed countries and already "generic" for several years. Furthermore, it should be noted that antibiotic resistance in Iran is a major and growing challenge, which has mostly been attributed to over usage of antibiotics and lack of drug resistance surveillance system.

As mentioned above, higher probability of patient's compliance with cefuroxime (compared to co-amoxiclav) could potentially contribute to minimizing the chance of antimicrobial resistance in our setting.

In summary, the results of this study demonstrated that 10 days of cefuroxime 250 mg BID is as clinically effective as 10 days of co-amoxiclav 500/125 mg TID in the treatment of acute sinusitis.

Keywords: acute sinusitis, cefuroxime, co-amoxiclav, Iran.

SUMMARY

Objectives. Acute sinusitis is a common upper respiratory tract infection worldwide, which can be severely complicated if inappropriate treatment is applied. The aim of this study was to assess and compare efficacy of cefuroxime and co-amoxiclav in the treatment of acute sinusitis in an Iranian sample population.

Methods. A randomized clinical trial, comparing the efficacy of two oral antibiotics, cefuroxime and co-amoxiclav in the treatment of acute sinusitis, was conducted in 2007. A total of 99 patients were enrolled in the study.

The clinical diagnosis of acute sinusitis was based on association of suborbital pain, purulent rhinorrhea and purulent discharge on the middle nasal meatus. All patients were also radiographically examined and their diagnoses were confirmed. Patients were randomly assigned to either receive 10 days of treatment with cefuroxime 250 mg twice daily (n=57) or receive co-amoxiclav 500/125 mg three times daily (n=42). Patients' responses to treatment were assessed during and at the end of the treatment.

Results. A satisfactory clinical outcome (cure or improvement of symptoms) was found in 86% (49/57) and 71.4% (30/42) of the clinically evaluable patients treated with cefuroxime or co-amoxiclav, respectively ($p > 0.05$).

Conclusions. The findings of this study suggest that cefuroxime (twice daily) is comparably effective as co-amoxiclav (three times a day) in the treatment of patients with acute sinusitis.

RIASSUNTO

Obiettivi. *La sinusite acuta è un'infezione delle alte vie respiratorie, diffusa in tutto il mondo, che può evolvere in complicanze anche gravi quando trattata in maniera inappropriata. Scopo del nostro studio è stato valutare e confrontare l'efficacia di cefuroxime e co-amoxiclav per il trattamento della sinusite acuta in una popolazione di pazienti in Iran.*

Metodi. *Lo studio clinico, randomizzato, di confronto dell'efficacia di cefuroxime e co-amoxiclav nel trattamento della sinusite acuta, è stato condotto nel 2007. Nello studio sono stati arruolati 99 pazienti.*

La diagnosi clinica di sinusite è stata posta sulla base di una associazione tra dolore sub-orbitale, rinorrea purulenta e secrezione purulenta dal meato nasale medio. Tutti i pazienti sono stati sottoposti a indagine radiografica che ne ha confermato la diagnosi. I pazienti sono stati randomizzati a ricevere, per 10 giorni, uno di due possibili trattamenti: cefuroxime 250 mg bid (n=57) o co-amoxiclav 500/125 mg tid (n=42). La risposta dei pazienti è stata valutata all'inizio e al termine del trattamento.

Risultati. *Un risultato favorevole (guarigione o miglioramento dei sintomi) è stato rilevato nell'86% (49/57) e nel 71,4% (30/42) dei pazienti clinicamente valutabili trattati con cefuroxime o co-amoxiclav, rispettivamente (p >0,05).*

Conclusioni. *I risultati del nostro studio suggeriscono che cefuroxime (due volte al giorno) presenta un'efficacia paragonabile a quella di co-amoxiclav (tre volte al giorno) nel trattamento di pazienti con sinusite acuta.*

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