

Effect of Ceftriaxone versus Amoxicillin + Clavulanic Acid for Treatment of Acute Bacterial Rhino Sinusitis: Short Course Therapy

Malath Azeez Al-Saadi^{1*}, Safaa Sahib Naji Sultan²

¹Pharmacology and Toxicology, College of Dentistry, University of Babylon, Hilla, Iraq; ²Surgery Department, College of Medicine, University of Babylon, Hilla, Iraq

Abstract

Citation: Al-Saadi MA, Sultan SSN. Effect of Ceftriaxone versus Amoxicillin+ Clavulanic Acid for Treatment of Acute Bacterial Rhino Sinusitis: Short Course Therapy. Open Access Maced J Med Sci. <https://doi.org/10.3889/oamjms.2018.329>

Keywords: Acute bacterial rhinosinusitis; Amoxicillin+clavulanic acid; Ceftriaxone

***Correspondence:** Malath Azeez Al-Saadi. Pharmacology and Toxicology, College of Dentistry, University of Babylon, Hilla, Iraq. E-mail: malathazez1122@gmail.com

Received: 27-Jul-2018; **Revised:** 22-Jul-2018;
Accepted: 27-Jul-2018; **Online first:** 16-Aug-2018

Copyright: © 2018 Malath Azeez Al-Saadi, Safaa Sahib Naji Sultan. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC 4.0)

Funding: This research did not receive any financial support

Competing Interests: The authors have declared that no competing interests exist

BACKGROUND: Acute bacterial rhinosinusitis is one of upper respiratory tract infection that disturbs patient life and requires special consideration.

AIM: To evaluate the efficiency of Ceftriaxone versus a high dose of Amoxicillin-clavulanic acid for the treatment of acute bacterial rhinosinusitis.

PATIENTS AND METHOD: Observational retrospective study include 120 patients of both sex classified into two groups equally conducted. G1 treated with Ceftriaxone 1 g intramuscular injection once daily while, G2 treated with oral Amoxicillin-clavulanic acid (875 mg/125 mg) twice daily for 3-4 days then, the outcome of treatment evaluated as a cure or failed at the fifth or fourth day of treatment.

RESULTS: Significant cure response observed in Ceftriaxone treated patient's $P \leq 0.05$ and significant failure response observed in Amoxicillin-clavulanic acid-treated patients when groups compared with each other. About gender and age groups, no significant differences in number between group 1 and 2 $P \geq 0.05$.

CONCLUSION: Ceftriaxone found more effective in the treatment of acute bacterial sinusitis than Amoxicillin+clavulanic acid. Amoxicillin+clavulanic acid associated with more male failure cases recorded than female.

Introduction

Rhinosinusitis is an inflammation of the lining epithelia of paranasal sinuses and nasal cavity associated with nasal purulent secretion [1] [2]. Rhinosinusitis classified to acute and chronic infection according to the duration of symptoms and to viral and bacterial rhinosinusitis depending on the causative source [3]. Symptoms are nasal congestion, purulent secretion, facial pain or pressure, pain on bending forward, upper teeth pain, fever and headache [4][5]. Acute rhinosinusitis among the principal cause to millions of physician visits every year [5]. The common cold is the common upper respiratory tract disease that could be complicated with bacterial

infection leading to acute bacterial rhinosinusitis [2] [6].

The inability of clinical criteria to distinguish between viral and bacterial rhinosinusitis cause inappropriate, excessive antibiotics prescription [6] [7].

Although most of the rhinosinusitis is of viral cause and self-limiting if symptoms persist for more than 10 days or worsen within 7 days regarded as acute bacterial rhinosinusitis [8]. According to that strategy of treatment changed to involve antibiotic treatments, topical corticosteroids, analgesics and/or decongestants [9].

However, proper antibiotics choice and duration are of great interest. Chose antibiotic prescription to depend on bacterial species, including

Streptococcus pneumoniae, *Haemophilus influenzae* and, particularly in children, *Moraxella catarrhalis* [10].

Guidelines of treatment suggest Amoxicillin-clavulanate as a first-line empiric antibiotic for mild rhino sinusitis short course treatment [11] [12]. In case of no improvement or penicillin sensitivity Amoxicillin-clavulanate dose either increased or another antibiotic selected like respiratory fluoroquinolone such as moxifloxacin, levofloxacin or cephalosporin's [12] [13].

Ceftriaxone is third-generation cephalosporin with strong wide range antibacterial profile, its β -lactam antibiotic act by inhibition of bacterial cell wall synthesis. Ceftriaxone half-life about eight hours allows single daily dose for treatment of infections caused by various bacterial species like *Klebsiella*, *Providencia*, *Serratia*, and *Haemophilus* species. It is the drug of choice for meningitis caused by *Haemophilus influenzae*. Adverse reaction of Ceftriaxone is hypersensitivity responses that are indistinguishable from those of penicillin [14].

Previous studies show that Ceftriaxone is good replacements for amoxicillin in the treatment of acute tonsillopharyngitis due to its safety [15].

The current study aims to evaluate the efficiency of Ceftriaxone versus oral Amoxicillin-clavulanic acid for the treatment of acute bacterial rhinosinusitis.

Patients and Method

A retrospective observational study conducted in (ear, nose and throat) ENT consultant clinic of our teaching hospital at a period from October 2016 to December 2017 for patients diagnosed with acute bacterial rhinosinusitis under the approval of a responsible, ethical committee of surgical department

A group of 120 patients of both sexes with age 15-52 years attend ENT consultant clinic suffering from facial pain and pressure, nasal obstruction with purulent discharge (rhinorrhoea) and fever after flu-like reaction for more than 10 days included according to Infectious Disease Society of America (IDSA) guidelines [12].

Patients with a history of flu-like illness without complication within the first 7 days, patients with previous surgery on nasal sinuses, patients with diabetes mellitus or renal impairment, patients with allergy to penicillin groups or ceftriaxone, patients with traumatic nasal injury, and symptoms duration more than 12 weeks excluded.

All patients included clinically examined by nasal endoscope finding the followings:

Nasal septal deviation, bilateral hypertrophy of inferior turbinate, pus discharge from middle meatus with red nasal mucosa and postnasal drip (mucus pus), then sent to computerised coronal tomography to ensure no complications.

Patients with a positive sign and symptoms of acute bacterial rhinosinusitis treated as the following:

Group 1: 60 patients prescribed with Ceftriaxone 1g intramuscular injection every 24 hours.

Group 2: 60 patients prescribed with Amoxicillin-clavulanic acid orally 1000 mg (875 mg/125 mg) every 12 hours for 3-4 days.

Xylometazoline nasal decongestant and analgesia prescribed for both groups.

After antibiotic regimen, patients followed up on the fifth day to evaluate the following:

1 - cure: no sign and symptoms of acute bacterial rhinosinusitis clinically.

2 - failure: persistence of sign and symptoms of acute bacterial rhinosinusitis clinically or complicated.

3 - an adverse reaction to the antibiotic regimen.

(Amoxicillin + clavulanic acid) oral tablet 1000 mg (875 mg/125 mg) (Comox Acino, Acino Pharma., Switzerland).

Ceftriaxone vial for intravenous /intramuscular injection 1 g (TORLAN, Spain).

Data presented by the proportion of the total number. Statistical significant assessed by Fisher exact test at the level of ≤ 0.05 using SPSS version 21 from IBM.

Results

The current study results show patients treated with Ceftriaxone for short course treatment have significantly higher cure proportion than those treated with (Amoxicillin + clavulanic acid) during follow up period, $P \leq 0.05$, Table 1.

Table 1: Response to treatments among groups

Treatments	Patients number	Gender		Cure cases	Failure cases
		Male	Female		
Ceftriaxone G1	60	34 (55.9%)	26 (44.06%)	50 (83.33%)*	10 (16.66%)
(Amoxicillin/clavulanic acid) G2	60	32 (53.3%)	28 (46.6%)	39 (65%)	21 (35%)*

* $p \leq 0.05$.

By gender, no significant differences in number between group 1 and 2, $P \geq 0.05$. Cure cases

about the gender of Ceftriaxone treated group show higher proportion among male than female, Table 2.

While in-group 2 the proportions of male and female were comparable in cure response, Table 3.

On the other hand, failure of treatment was more in male than female in group 2, Table 3.

About age group, no differences in numbers of patients observed between treatments groups, Table 2 and 3.

Table 2: Response to treatments of group 1 about gender and age group

Age group	Male	Female
20-30 years	25 (42.3%)	19 (31.66%)
30-40	5 (8.47%)	5 (8.47%)
40-60	3 (5%)	3 (5%)
Cure cases	27 (81.8%)	23 (84.61%)
Failure cases	6 (18.18%)	4 (15.38%)

Three patients develop skin rash adverse reaction to Ceftriaxone while only one patient develop a skin reaction to Amoxicillin+ clavulanic acid treatment recorded during the study period.

Failure cases treated by the change of antibiotic regimen or surgical treatment for those complicated during the study period according to clinical examination at follow up visit.

Table 3: Response to treatments of group 2 about gender and age group

Age group	Male	Female
20-30 years	21 (35%)	19(31%)
30-40	8 (13.3%)	6(10%)
40-60	3 (5%)	3(5%)
Cure cases	19 (59.37%)	20(71.4%)
Failure cases	13 (40.6%)	8(28.57%)

Discussion

Acute bacterial rhinosinusitis among the higher complaints of patients attends ENT outpatient clinics in our region. It disturbs the patient's normal life with serious complication if not treated properly [16].

The current study was a retrospective observational study that aimed to evaluate the response of patients with acute bacterial rhinosinusitis to two regimens of antibiotics including first-line oral (Amoxicillin + clavulanic acid) drug in high dose and Ceftriaxone.

Short antibiotic treatment decided to avoid an adverse reaction, development of bacterial resistance and decrease cost; depending on previous studies that found no dependable differences in response between short and long antibiotic treatment [12] [17].

The choice of Ceftriaxone was following recent guidelines that suggest β -lactam agent rather than a respiratory fluoroquinolone for empiric antimicrobial therapy [12].

Beside to Ceftriaxone efficiency against *Haemophilus* species and other pathogenic bacteria which are mostly isolated species from swaps of acute bacterial rhinosinusitis patients and its recorded safety for short course treatments that decrease patients hospitalisation and cost [18].

The study results show significant high cure response to Ceftriaxone than (Amoxicillin + clavulanic acid) as observed at the end of 3-4 days of treatments according to guidelines of short course antibiotic treatments. This result proves the efficiency of Ceftriaxone for acute bacterial rhinosinusitis. Although its parenteral drug, it's well tolerated with broad spectrum efficiency that made Ceftriaxone good alternative antibiotic. This explanation goes with Seaton and Barr [18] study that evaluate outpatient parenteral antibiotic therapy to decrease hospital admission and cost. Also, agree with Duncan and colleague study [15] that found Ceftriaxone excellent broad-spectrum antibiotic for various clinical infection states including upper respiratory tract infection.

Moreover, high failure response to (Amoxicillin + clavulanic acid) observed in this study even though it regarded as the first-line drug for acute bacterial rhinosinusitis could be explained by the development of non B- lactamase type of resistance in certain pathogenic species like *Streptococcus pneumonia* making Ceftriaxone more efficient replacement [19] [20].

However, it required future microbiological study to look for the most common causative microorganism for acute bacterial rhinosinusitis in our region.

This finding unlike Muhammad and colleague [21] finding that demonstrate the effectiveness of high dose Amoxicillin + clavulanic acid in the treatment of acute bacterial rhinosinusitis as compared to levofloxacin for 10 days treatment, Which may be due to the dissimilarity of treatment period that lasts for 3-4 days in the current study.

About gender response to treatment, male treated with Ceftriaxone show more resolution of symptoms (cure) as compared to female patients, that probably due to differences in some included cases. While, in group 2, male patients show more failure response than the female of the same group that could be due to the variation of an inhabitant of a respiratory microorganism or due to variation in immune response and tolerance between male and female [22] [23].

The antibiotic-related adverse reaction was predicted for the types of antibiotic used with more adverse reaction recorded in group 1 [24] although, it is not serious reactions.

Nasal decongestant and analgesics prescribed for both treatment groups to decrease nasal obstruction and relief painful symptoms associated with acute bacterial rhinosinusitis.

In conclusion, Ceftriaxone found to be more effective than Amoxicillin + clavulanic acid in the treatment of acute bacterial sinusitis. Amoxicillin + clavulanic acid associated with more male failure cases than female.

References

- Meltzer EO, Hamilos DL, Hadley JA, Lanza DC, Marple BF, Nicklas RA, et al. Rhinosinusitis: establishing definitions for clinical research and patient care. *Otolaryngol Head Neck Surg.* 2004; 131(6)(Suppl):S1-S62. <https://doi.org/10.1016/j.otohns.2004.09.067> PMID:15577816
- Lacroix JS, Ricchetti A, Lew D, Delhumeau C, Morabia A, Stalder H, Terrier F, Kaiser L. Symptoms and clinical and radiological signs predicting the presence of pathogenic bacteria in acute rhinosinusitis. *Acta oto-laryngologica.* 2002; 122(2):192-6. <https://doi.org/10.1080/00016480252814216> PMID:11936912
- Fleming-Dutra KE, Hersh AL, Shapiro DJ, Bartoces M, Enns EA, File TM, Finkelstein JA, Gerber JS, Hyun DY, Linder JA, Lynfield R. Prevalence of inappropriate antibiotic prescriptions among US ambulatory care visits, 2010-2011. *Jama.* 2016; 315(17):1864-73. <https://doi.org/10.1001/jama.2016.4151> PMID:27139059
- Piccirillo JF. Clinical practice. Acute bacterial sinusitis. *N Engl J Med.* 2004; 351(9):902-910. <https://doi.org/10.1056/NEJMcip035553> PMID:15329428
- Hwang PH. A 51-year-old woman with acute onset of facial pressure, rhinorrhea, and tooth pain: review of acute rhinosinusitis. *JAMA.* 2009; 301(17):1798-1807. <https://doi.org/10.1001/jama.2009.481> PMID:19336696
- Fokkens WJ, Lund VJ, Mullol J, Bachert C, Alobid I, Baroody F, Cohen N, Cervin A, Douglas R, Gevaert P, Georgalas C. EPOS 2012: European position paper on rhinosinusitis and nasal polyps 2012. A summary for otorhinolaryngologists. *Rhinology.* 2012; 50(1):1-2. PMID:22469599
- Smith SS, Evans CT, Tan BK, Chandra RK, Smith SB, Kern RC. National burden of antibiotic use for adult rhinosinusitis. *J Allergy Clin Immunol.* 2013; 132:1230-1232. <https://doi.org/10.1016/j.jaci.2013.07.009> PMID:23987794 PMID:PMC3815964
- Blackwell DL, Lucas JW, Clarke TC. Summary health statistics for U.S. adults: national health interview survey, 2012. *Vital Health Stat.* 2014; 10:1-171.
- Hoffmans R, Schermer T, Van WC, Fokkens W. Management of rhinosinusitis in Dutch general practice. *Prim Care Respir J.* 2011; 20(1):64-70. <https://doi.org/10.4104/pcrj.2010.00064> PMID:21311844
- Benninger MS, Payne SC, Ferguson BJ, Hadley JA, Ahmad N. Endoscopically directed middle meatal cultures versus maxillary sinus taps in acute bacterial maxillary rhinosinusitis: a meta-analysis. *Otolaryngology—Head and Neck Surgery.* 2006; 134(1):3-9. <https://doi.org/10.1016/j.otohns.2005.10.010> PMID:16399172
- Anon JB, Jacobs MR, Poole MD, Ambrose PG, Benninger MS, Hadley JA, et al. Antimicrobial treatment guidelines for acute bacterial rhinosinusitis. *Otolaryngol Head Neck Surg.* 2004; 130(1):1-45. PMID:14726904
- Chow AW, Benninger MS, Brook I, L. Brozek, Ellie J. C. Goldstein, L. A. Hicks et al. Infectious Diseases Society of America. IDSA clinical practice guideline for acute bacterial rhino sinusitis in children and adults. *Clin Infect Dis.* 2012; 54(8):e72-e112. <https://doi.org/10.1093/cid/cis370> PMID:22438350
- Desrosiers M, Evans GA, Keith PK, Wright ED, Kaplan A, Bouchard J, Ciavarella A, Doyle PW, Javer AR, Leith ES, Mukherji A. Canadian clinical practice guidelines for acute and chronic rhinosinusitis. *Allergy, Asthma & Clinical Immunology.* 2011; 7(1):2. <https://doi.org/10.1186/1710-1492-7-2> PMID:21310056 PMID:PMC3055847
- Laurence L. Brunton, Bruce A. Chabner and Björn C. Knollmann. Goodman & Gilman's The Pharmacological Basis of Therapeutics. McGraw-Hill library e-book. 12th edition, 2011:1342-1345.
- Duncan CJ, Barr DA, Seaton RA. Outpatient parenteral antimicrobial therapy with ceftriaxone, a review. *Int J Clin Pharm.* 2012; 34(3): 410-417. <https://doi.org/10.1007/s11096-012-9637-z> PMID:22527482
- Al Alawi S, Abdulkarim S, Elhennawy H, Al-Mansoor A, Al Ansari A. Outpatient parenteral antimicrobial therapy with ceftriaxone for acute tonsillopharyngitis: efficacy, patient satisfaction, cost effectiveness, and safety. *Infection and Drug Resistance.* 2015; 8:279-285. PMID:26300650 PMID:PMC4536842
- Mihani J, Këlliçi S. Patterns of Antibiotic Prescription in Children: Tirana, Albania Region. *Open Access Maced J Med Sci.* 2018; 6(4):719. <https://doi.org/10.3889/oamjms.2018.150> PMID:29731947 PMID:PMC5927510
- Seaton, Barr DA. Outpatient parenteral antibiotic therapy: principles and practice. *Eur J Intern Med.* 2013; 24(7):617-23. <https://doi.org/10.1016/j.ejim.2013.03.014> PMID:23602223
- Cohen R, Navel M, Grunberg J, Boucherat M, Geslin P, Derriennic M, Pichon F, Goehrs JM. One dose ceftriaxone vs. ten days of amoxicillin/clavulanate therapy for acute otitis media: clinical efficacy and change in nasopharyngeal flora. *The Pediatric infectious disease journal.* 1999; 18(5):403-9. <https://doi.org/10.1097/00006454-199905000-00002> PMID:10353511
- Bucher HC, Tschudi P, Young J, Périat P, Welge-Lüssen A, Züst H, Schindler C. Effect of Amoxicillin-Clavulanate in Clinically Diagnosed Acute Rhinosinusitis A Placebo-Controlled, Double-blind, Randomized Trial in General Practice. *Arch Intern Med.* 2003; 163(15):1793-1798. <https://doi.org/10.1001/archinte.163.15.1793> PMID:12912714
- Muhammad R, Zaman A, Khan Z, Khan AR. Comparison of efficacy of amoxicillin clavulanate and levofloxacin in treatment of acute bacterial sinusitis. *Journal of Medical Sciences.* 2015; 23(2):77-81.
- Muenchhoff M, Goulder PJ. Sex differences in pediatric infectious diseases. *The Journal of infectious diseases.* 2014; 209(Suppl 3):S120-6. <https://doi.org/10.1093/infdis/jiu232> PMID:24966192 PMID:PMC4072001
- Falagas ME, Mourtoukou EG, Vardakas KZ. Sex differences in the incidence and severity of respiratory tract infections. *Respiratory medicine.* 2007; 101(9):1845-63. <https://doi.org/10.1016/j.rmed.2007.04.011> PMID:17544265
- Thomson SR, Ommurugan B, Patil N. Ceftriaxone Induced Hypersensitivity Reactions Following Intradermal Skin Test: Case Series. *Journal of Clinical & Diagnostic Research.* 2017; 11(10). <https://doi.org/10.7860/JCDR/2017/29088.10758>