International Journal of Research in Health and Allied Sciences

Journal home page: www.ijrhas.com

Official Publication of "Society for Scientific Research and Studies" [Regd.]

ISSN: 2455-7803

Original Research

Comparative effectiveness of amoxicillin versus amoxicillin-clavulanate among adults with acute sinusitis

Dr. Sumit Walia[1], Dr. Vikrant Singh Ghiyali[2]

[1]Medical officer (ENT), Regional hospital kullu, Himachal Pradesh
[2]Medical Officer (ENT), Civil Hospital Rohru, Shimla Himachal Pradesh

ABSTRACT:
Aim: To compare the effectiveness of amoxicillin-clavulanate versus amoxicillin for adults diagnosed with acute sinusitis (AS). **Material and Methods**: Adults with AS who were administered amoxicillin and clavulanate underwent a retrospective cohort study. Return visits for sinusitis associated with amoxicillin versus amoxicillin-clavulanate were the main outcome. Hospitalisations, gastrointestinal-related adverse events (AEs), and 30-day infectious complications were all secondary outcomes. Models using logistic regression and propensity score matching were adjusted for relevant confounders. **Results**: There were 100 AS patient visits total, of which 29 had amoxicillin and 71 had amoxicillin and clavulanate prescribed. 75, 75% of the patients were men. There was no difference between amoxicillin (7%) and amoxicillin/clavulanate (8%), in terms of repeat visits due to sinusitis. Amoxicillin had a lower rate of gastrointestinal adverse events (AEs) than amoxicillin and clavulanate (2%). **Conclusion**: With less gastrointestinal side effects, amoxicillin showed equivalent efficacy to amoxicillin/clavulanate for AS. When an adult with AS meets the criteria for antibiotic therapy, amoxicillin is a good option.
Keywords: adverse drug event, amoxicillin-clavulanate, antimicrobial stewardship, clinical outcomes, outpatient, sinusitis.

Received: 12 November, 2022 Accepted: 18 November, 2022

Corresponding Author: Dr. Vikrant Singh Ghiyali, Medical Officer (ENT), Civil Hospital Rohru, Shimla Himachal Pradesh

This article may be cited as: Walia S, Ghiyali VS. Comparative effectiveness of amoxicillin versus amoxicillin-clavulanate among adults with acute sinusitis. Int J Res Health Allied Sci 2022; 8(6):70- 72

INTRODUCTION

Acute rhinosinusitis affects 1 in 8 adults in the United States, culminating in almost 30 million annual cases. Most cases are of viral etiology; but, in a subset of rhinosinusitis cases where specific criteria are met, a probable bacterial infection warrants antibiotic use.[1,2] Infectious Diseases Society of America (IDSA) guidelines recommend 3 criteria where antibiotics are indicated: (1) persistent symptoms and not improving (≥10 days), (2) worsening symptoms (eg, new onset fever, nasal discharge/cough), or (3) severe symptoms (eg, purulent nasal discharge or pain lasting ≥3 days or high fever ≥102°F).[3] The American College of Emergency Physicians also recommends limiting antibiotic treatment to patients meeting similar criteria.[4]

Acute rhinosinusitis accounts for 1 in 5 antibiotic prescriptions for adults, making it the fifth most common reason for an antibiotic prescription. Approximately 6% to 7% of children with respiratory symptoms have acute rhinosinusitis. An estimated 16% of adults are diagnosed with ABRS annually. Given the clinical nature of this diagnosis, there is a possibility of overestimation.

An estimated 0.5 to 2.0% of viral rhinosinusitis (VRS) will develop into bacterial infections in adults and 5 to 10% in children.[5,6]

The American Academy of Pediatrics Clinic Practice Guideline for the Diagnosis and Management of Acute Bacterial Sinusitis in Children Aged to 18 Years recommends amoxicillin with or without clavulanate as first-line therapy. The duration of treatment is unclear, however treating for an additional seven days after symptoms resolve was their suggestion. The criteria for treatment failure is if symptoms do not decrease or worsen after 72 hours of therapy. If the patient cannot tolerate oral fluids, then the patient can receive ceftriaxone 50m/kg. If the patient can tolerate oral fluids the next day and improves, then the patient can transition to an oral

antibiotic course thereafter. A separate article recommended amoxicillin with clavulanate as initial therapy in children to adequately cover beta-lactamase-producing pathogens.[7] Hence, this study was conducted to compare the effectiveness of amoxicillin versus amoxicillin-clavulanate among adults with acute sinusitis.

Material and methods

In total, 100 participants were used in this investigation. Demographic information included the patient's sex, age, temperature at the index visit, and a few comorbidities (such as cancer, immunosuppression, hemodialysis, and chronic obstructive pulmonary disease). Diagnostic codes or drugs prescribed particularly for certain illnesses were used to identify comorbidities. A fresh outpatient visit with an acute sinusitis diagnostic code within 30 days of the index visit was considered a return visit for acute sinusitis. A new outpatient or inpatient diagnostic code for these illnesses within 30 days of the index visit detected potential infectious consequences (i.e., Clostridioides difficile infections, pneumonia, meningitis, mastoiditis, or face cellulitis).
If the patient did not have a similar diagnostic code within the six months prior to the visit, return visits for gastrointestinal-related adverse antibiotic events were identified by outpatient visits or inpatient admissions with diagnostic codes consistent with potential gastrointestinal-related adverse antibiotic events (e.g., diarrhoea, colitis, hepatitis, nausea) for visits that occurred within 14 days of the index acute sinusitis visit. An admittance date that occurred between one and thirty days after the index visit served as the definition of a hospitalisation. For the purpose of accounting for potential antibiotic therapy confounders, a matched propensity score technique was employed. Patients who received an amoxicillin and clavulanate prescription were compared to those who received an amoxicillin only prescription.

Results

A total of 100 AS patient visits were identified: 29 prescribed amoxicillin and 71 amoxicillin-clavulanate. Most patients were male (75, 75%). There was no difference in sinusitis-related return visits between amoxicillin (7%) and amoxicillin-clavulanate (8%). Gastrointestinal-related AEs were lower with amoxicillin (1%) relative to amoxicillin-clavulanate (2%).

Table 1: gender wise distribution of subjects

Gender	Number of subjects	Percentage
Males	75	75%
Females	25	25%
Total	100	100%

Table 2: Number of subjects in the two groups

Groups	Number of subjects	Percentage
Amoxicillin group	29	29%
Amoxicillin-clavulanate group	71	71%
Total	100	100%

Patients who received amoxicillin had lower rates of comorbidities, lower rates of high fever, and higher rates of receiving treatment from a non-physician healthcare provider than those who received amoxicillin and clavulanate.

Discussion

In this large retrospective cohort study of adults with acute sinusitis, there were no differences in return visits or infectious complications between amoxicillin and amoxicillin-clavulanate treatment. However, Clostridiodes difficile and gastrointestinal adverse events were significantly higher in patients treated with amoxicillin-clavulanate as compared with amoxicillin. Further, we observed a reduction in infectious complications and hospitalizations in patients that received antibiotics compared with no antibiotics. Explanations for the lack of observed difference in treatment outcomes between amoxicillin and amoxicillin-clavulanate highlight the relatively low prevalence of infectious complications overall and the diminished importance of pathogens other than Streptococcus pneumoniae.
As sinus aspiration for uncomplicated acute sinusitis is uncommon, we were not able to determine microbial etiology within the cohort. Although the diagnosis of gastrointestinal-related adverse antibiotic events was low, only conditions serious enough to warrant revisit or admission to the hospital were captured. Some clinical trials and postmarketing studies suggest that amoxicillin-clavulanate gastrointestinal toxicity incidence is twice that of amoxicillin (13% vs 7%).[8] Clavulanate also appears to reduce beneficial microbiota relative to amoxicillin alone, which may contribute to the observed increase in Clostridiodes difficile infections.[9]
In a study by Rovelsky SA et al[10], a total of 89,627 AS patient visits were identified: 18,576 prescribed amoxicillin and 71,051 amoxicillin-clavulanate. Most patients were male (75,604; 84.4%) and afebrile (80,624; 91.7%). The propensity score-matched cohort comprised 17,929 amoxicillin and 42,294 amoxicillin-clavulanate patient visits. There was no difference in sinusitis-related return visits between amoxicillin (4.9%) and amoxicillin-clavulanate (5.1%) (adjusted odds ratio [OR], 0.96; 95% confidence interval [CI], 0.88, 1.04; P = 0.317). Infectious complications (amoxicillin [0.3%] vs amoxicillin-clavulanate [0.4%]); (adjusted OR, 0.78; 95% CI, 0.57, 1.07; P = 0.124) and hospitalization (amoxicillin [2.0%] vs amoxicillin-clavulanate [2.4%]); (adjusted OR, 0.92; 95% CI, 0.81, 1.04; P =

0.173) were not different. Gastrointestinal-related AEs were lower with amoxicillin (0.5%) relative to amoxicillin-clavulanate (0.7%); (adjusted OR, 0.67; 95% CI, 0.53, 0.86; P = 0.002). Comorbidity was the only guideline-recommended risk factor that was a significant predictor of infectious complications with respect to treatment (amoxicillin vs amoxicillin-clavulanate, OR, 0.63; 95% CI, 0.40 to 0.94; P = 0.022). It was concluded that Amoxicillin demonstrated similar efficacy to amoxicillin-clavulanate for AS with fewer gastrointestinal-related AEs.

In a study by Gregory J et al[11], it was evaluated if high-dose amoxicillin plus clavulanate (with double the amount of amoxicillin) was superior to standard-dose amoxicillin plus clavulanate in adults. This was a double-blind, comparative-effectiveness randomized clinical trial. Participants included adults aged 18 years or older who were prescribed amoxicillin plus clavulanate for acute bacterial sinusitis diagnosed in accordance with the Infectious Diseases Society of America guidelines. Amoxicillin 875 mg with clavulanate 125 mg plus either placebo (standard dose) or amoxicillin 875 mg (high dose) twice a day for 7 days was administered. At an unplanned interim analysis prompted by COVID-19 restrictions, 157 of a projected 240 participants had been enrolled (mean age, 48.5 [range, 18.7-84.0] years; 117 women [74.5%]), with 79 randomized to the standard dose and 78 to the high dose; 9 and 12, respectively, withdrew or were lost to follow-up before the assessment of the primary outcome. At day 3, 31 of 70 participants (44.3%) in the standard-dose group reported a global rating of "a lot better" or "no symptoms," as did 24 of 66 (36.4%) in the high-dose group, for a difference of -7.9% (95% CI, -24.4% to 8.5%; P = .35). The study was, therefore, stopped for futility. Diarrhea was common in both groups by day 3, with any diarrhea reported in 29 of 71 participants (40.8%) receiving the standard dose and 28 of 65 (43.1%) receiving the high dose and severe diarrhea reported in 5 of 71 (7.0%) and 5 of 65 (7.7%), respectively. The results of this randomized clinical trial suggested that adults treated for clinically diagnosed acute sinusitis did not appear to benefit from taking high-dose compared with standard-dose amoxicillin plus clavulanate.

Hence, this study was conducted to compare the effectiveness of amoxicillin versus amoxicillin-clavulanate among adults with acute sinusitis.

Conclusion

With less gastrointestinal side effects, amoxicillin showed equivalent efficacy to amoxicillin/clavulanate for AS. When an adult with AS meets the criteria for antibiotic therapy, amoxicillin is a good option.

References

1. Villarroel MA, Blackwell DL, Jen A, Tables of Summary Health Statistics for U.S. Adults: 2018 National Health Interview Survey. National Center for Health Statistics. 2019.
2. Fleming-Dutra KE, Hersh AL, Shapiro DJ, et al. Prevalence of inappropriate antibiotic prescriptions among US ambulatory care Visits, 2010–2011. JAMA. 2016;315(17):1864-1873.
3. Chow AW, Benninger MS, Brook I, et al. Executive summary: IDSA clinical practice guideline for acute bacterial rhinosinusitis in children and adults. Clin Infect Dis. 2012;8(54):1041-1045.
4. American College of Emergency Physicians. Choosing Wisely. Avoid prescribing antibiotics in the emergency department for uncomplicated sinusitis. 2014.
5. Aring AM, Chan MM. Current Concepts in Adult Acute Rhinosinusitis. Am Fam Physician. 2016 Jul 15;94(2):97-105.
6. DeMuri G, Wald ER. Acute bacterial sinusitis in children. Pediatr Rev. 2013 Oct;34(10):429-37.
7. Brook I. Acute sinusitis in children. Pediatr Clin North Am. 2013 Apr;60(2):409-24.
8. Salvo F, De sarro A, Caputi AP, et al. Amoxicillin and amoxicillin plus clavulanate: a safety review. *Expert Opin Drug Saf*. 2009;8(1):111-118.
9. Espinosa-Gongora C, Jessen LR, Kieler IN, et al. Impact of oral amoxicillin and amoxicillin/clavulanic acid treatment on bacterial diversity and β-lactam resistance in the canine faecal microbiota. *J Antimicrob Chemother*. 2020;75(2):351-361.
10. Rovelsky SA, Remington RE, Nevers M, Pontefract B, Hersh AL, Samore M, Madaras-Kelly K. Comparative effectiveness of amoxicillin versus amoxicillin-clavulanate among adults with acute sinusitis in emergency department and urgent care settings. J Am Coll Emerg Physicians Open. 2021 Jun 16;2(3):e12465.
11. Gregory J, Huynh B, Tayler B, Korgaonkar-Cherala C, Garrison G, Ata A, Sorum P. High-Dose vs Standard-Dose Amoxicillin Plus Clavulanate for Adults With Acute Sinusitis: A Randomized Clinical Trial. JAMA Netw Open. 2021 Mar 1;4(3):e212713.