Original Article

Empiric Antibiotic Therapy in the Treatment of Community-acquired Pneumonia in a General Hospital in Saudi Arabia

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Abstract

Background: Guideline-based empiric antimicrobial therapy is recommended for the treatment of community-acquired pneumonia (CAP). In this study, we evaluate the pattern of empiric antibiotics of CAP patients. **Materials and Methods:** Patients with CAP were retrieved from the health information unit using the International Classification of Diseases, Ninth Revision. The electronic pharmacy database was used to retrieve prescribed antibiotics and the duration of therapy for each antibiotic. **Results:** A total of 1672 adult patients were included in the study and 868 (52%) were male. Of all the patients, 47 (2.8%) were admitted to the intensive care unit (ICU). The most frequently used antibiotics were levofloxacin (68.12%), ceftriaxone (37.7%), imipenem-cilastatin (32.5%), and azithromycin (20.6%). The mean days of therapy of each of these antibiotics were 3.2, 2.8, 4.4, and 2.9, respectively. A combination therapy of levofloxacin and imipenem-cilastatin was prescribed for 355 (21.8%) of non-ICU patients versus 20 (60.6%) of ICU patients ($P = 0.0007$). Imipenem-cilastatin was prescribed for 518 (31.8%) of non-ICU patients versus 25 (56.8%) of ICU patients ($P = 0.0009$). Levofloxacin was prescribed for 1106 (68%) of non-ICU patients versus 33 (75%) of ICU patients ($P = 0.412$). Ceftriaxone use decreased significantly from 40.9% in 2013 to 25.9% in 2016 ($P = 0.034$). In addition, levofloxacin use increased from 63.7% to 75% ($P = 0.63$). **Conclusion:** The most commonly used antibiotics were levofloxacin, ceftriaxone, imipenem-cilastatin, and azithromycin. The data call for further refinement and prospective audit of antibiotic use in CAP, especially in non-ICU settings.

Keywords: Antimicrobial stewardship, antimicrobial therapy, community-acquired pneumonia, empiric antibiotic

Introduction

Community-acquired pneumonia (CAP) is an important admission diagnosis with an annual admission of 664 patients in our hospital,[1] with an annual rate of 44/1000 patients. Guideline-based empiric antimicrobial therapy is recommended for the treatment of CAP by the American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA).[2] Few studies examined different aspects of CAP in Saudi Arabia.[3-6] Limited data regarding the adherence to ATS/IDSA guidelines are available from this part of the world. One study included patients from the United Arab Emirates, Kuwait, Bahrain, Oman, and Qatar[7] and one study from Oman only[8] evaluated the adherence to the Gulf Cooperation Council (GCC) CAP guidelines.[4] In this study, we evaluate the rate of CAP patients who received the recommended antibiotics based on local and international guidelines.[2,4] In addition, we evaluate the trend over time of the use different antibiotics and the use of combination therapy.

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Materials and Methods

This is a retrospective chart review of adults with CAP who were admitted to a general hospital in Saudi Arabia from March 2013 to June 2016. The hospital is a 350-bed general hospital and provides medical care for 160,000 individuals eligible

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for medical care.[9] The patients' data were retrieved from the health information unit using the International Classification of Diseases, Ninth Revision (ICD-9). The electronic pharmacy database was then used to retrieve the prescribed antibiotics and the duration of therapy for each antibiotic. A standard Microsoft Excel sheet was used to record the retrieved data. Statistical analysis was done using Minitab® (Minitab Inc. Version 17, State College, Pennsylvania, USA; 2017). The generated data included the mean duration of each antibiotic standard deviation (±SD). A significant *P* value was considered if $P < 0.05$. The study was approved by the JHAH Institutional Review Board. The diagnosis of CAP was based on the presence of a group of clinical features such as fever and the demonstration of an infiltrate by chest radiograph with or without supporting microbiological data as suggested by the ATS/IDSA.[2] We also calculated the CURB-65 score based on Confusion, Blood Urea, Respiratory Rate, Blood pressure, and age ≥65 years.

Results

A total of 1672 adult patients were admitted during the study period. Of those patients, 868 (52%) were male. Of all patients, 47 (2.8%) were admitted initially to the intensive care unit (ICU). The mean CURB-65 score (confusion, blood urea, respiratory rate, blood pressure, and age > 65 years) (±SD) was 1.47 (1.15) and 1.8 (0.92) for patients who did not require ICU and those who required ICU admission ($P = 0.019$). The most frequently used antibiotics as single agents or combined with other antibiotics were levofloxacin (68.12%); ceftriaxone (37.7%), imipenem-cilastatin (32.5%), and azithromycin (20.6%). The mean days of the use of these antibiotics were 3.2, 2.8, 4.4, and 2.9, respectively [Figure 1]. The overall mean (±SD) days of therapy of antibiotics was 5.96 (±4.8) and a median of 5 days [Figure 2].

A combination therapy of levofloxacin and imipenem-cilastatin was prescribed for 355 (21.8%) of non-ICU patients versus 20 (60.6%) of ICU patients ($P = 0.0007$). Levofloxacin was prescribed for 1106 (68%) of non-ICU patients versus 33 (75%) of ICU patients ($P = 0.412$). Imipenem-cilastatin was prescribed for 518 (31.8%) of non-ICU patients versus 25 (56.8%) of ICU patients ($P = 0.0009$). There was no relationship between antibiotic use and the CURB-65 score [Figure 3].

There was no time-trend difference in the percentage of patients receiving imipenem-cilastatin (34.6%) and azithromycin (21.7%–18.3%) [Figure 4]. However, ceftriaxone use decreased from 41% in 2013 to 26% in 2016 ($P = 0.034$). In addition, levofloxacin use increased from 63.7% to 75% ($P = 0.63$).

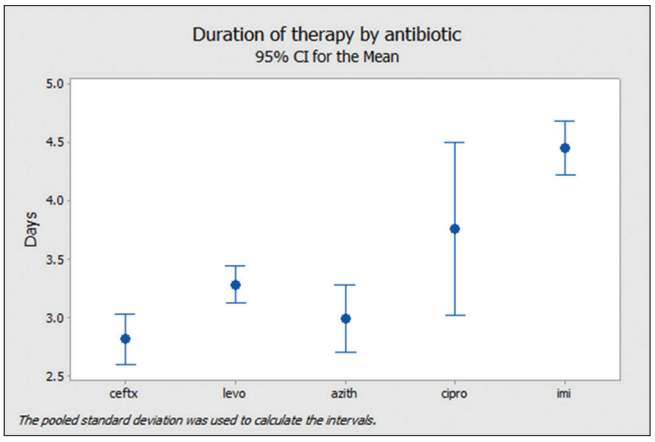

Figure 1: Box blot of the mean and the 95% confidence interval of the duration of commonly used antibiotics (the number of cases in each antibiotic is as follows: Ceftriaxone (ceftx, 631); levofloxacin (levo, 1139); azithromycin (azith, 344); ciprofloxacin (cipro, 54); imipenem (imi, 543)

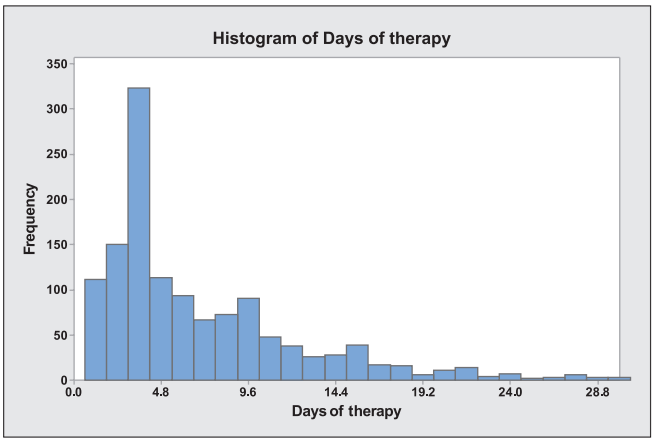

Figure 2: A histogram showing the days of therapy of antibiotics of the included patients

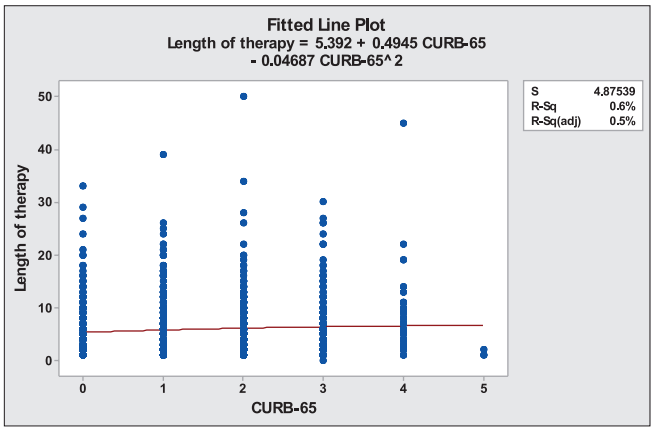

Figure 3: A fitted line blot of the length of antimicrobial therapy and the CURB-65 score

Discussion

This is the largest study from the Gulf region to investigate antimicrobial therapy of admitted CAP patients. Two previous smaller studies addressed this issue and one of them was a multicenter.[7,8] The current study showed that combination therapy of levofloxacin and imipenem-cilastatin was prescribed for 21.8% of non-ICU patients compared to 60.6% of ICU patients and that imipenem-cilastatin was prescribed for 31.8%

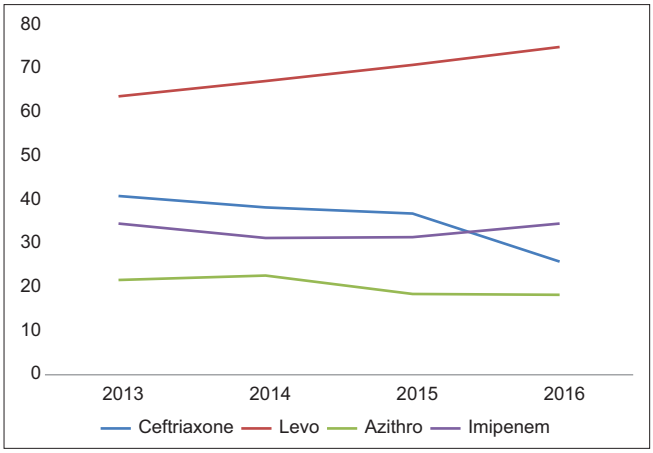

Figure 4: Percentage of patients receiving specified antibiotics per year of admission

of non-ICU patients compared to 56.8% of ICU patients. The overall empiric antibiotic use in CAP in the current study was in alignment with those of the ATS/IDSA.[2] Various studies showed that the overall guideline adherence rate for empiric antibiotic therapy for CAP was 31.2%–48%.[10-12] The compliance rate of empiric antibiotic use in CAP was very low (6.4%) in one study from Europe in 2006[13] and was 66% in a study from South Africa.[14] Adherence to CAP guidelines was associated with better prognosis in the short term, especially in patients requiring mechanical ventilation.[15] The rate of initial ICU admission of CAP patients was low (2.8%) in the present study. This rate is comparable to the rate from Hong Kong (4%) and lower than rates from Spain (17%) and United Kingdom (8.7%).[16,17] However, rates of ICU admission and criteria leading to such admissions may be different among multiple healthcare systems.[18] One study showed that the most common antibiotics used were levofloxacin, amoxicillin-clavulanic acid, and clarithromycin.[13] In a study from China, levofloxacin was the most common initial antibiotic (15.7%).[19] In one study, non-ICU patients received a respiratory fluoroquinolone alone 33% of the time or beta-lactam plus macrolide (19%).[20] In an Australian study, ceftriaxone and azithromycin combination was used for 56% of the patients[21] and one-third of patients with CAP in an Indian study received macrolide and a beta-lactam.[22]

In the current study, imipenem-cilastatin was prescribed for about one-third of non-ICU patients and for over half of ICU patients ($P = 0.0009$). The data suggest that there is room to improve empiric antibiotic usage in non-ICU settings. In an Australian study, many mild CAP patients were treated as a severe CAP with an odds ratio of 8 for mild CAP versus severe CAP.[21] Moreover, in an audit from Britain, initial antibiotics matched local CAP guidelines in only 55.5% of patients.[23] In addition, in one study from the GCC countries, 20.3% of 684 patients were treated with two agents and levofloxacin was the most frequently used (65.7%), followed by ceftriaxone (16.1%) and moxifloxacin (13.1%).[7] Thus, despite the existence of guidelines, the optimal use of antibiotics had not been achieved in CAP. Prospective audit and feedback for the use of antibiotics are still a priority to improve antibiotic stewardship.

In the United States, it was observed that the use of macrolides increased from 20% in 1993 to 30% in 2006 ($P < 0.001$) and an increase in quinolones from 0% to 39% from 1993 through 2008 ($P < 0.001$).[24] We found no change in the prescribing pattern of azithromycin and imipenem-cilastatin, and there was a significant decrease in ceftriaxone paralleled by an increase in levofloxacin use. Previous studies from Saudi Arabia did not address the rate of *Streptococcus pneumoniae* resistance to quinolone[25,26] or showed a very low resistance rate.[27] Thus, further studies are needed to examine the change in *S. pneumoniae* resistance to quinolones in this part of the world. Antibiotic duration and adherence to CAP guidelines are important elements in antibiotic stewardship.[28] According to the IDSA guidelines, a minimum of 5 days is needed to treat patients with CAP.[2] The mean duration of therapy of each antibiotic was 2.8–4.4 days, with mean antibiotic days of 7 ± 5 days.

This study has limitations and includes retrospective nature, a single-center study, and the lack of microbiological data. In addition, we depended on ICD coding and did not check the CAP diagnosis using the medical charts. Thus, this is an additional limitation of the study since a misclassified CAP diagnosis may explain some of the noncompliance to guidelines. It is known that there is a wide gap in guideline recommendations and actual usage pattern of antibiotics. Moreover, that this study looked at the gap in practice and compared the data to other parts of the world to highlight any discrepancies to rectify and improve the adherence to antibiotics as per the guidelines for CAP.

Conclusion

There is a room for further antibiotic stewardship in the area of CAP and further refine and prospective audit of antibiotic use in CAP, especially in non-ICU settings.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Al-Tawfiq JA, Rabaan AA, Hinedi K. Influenza is more common than Middle East respiratory syndrome coronavirus (MERS-coV) among hospitalized adult Saudi patients. Travel Med Infect Dis 2017;20:56-60.
2. Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, *et al.* Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis 2007;44 Suppl 2:S27-72.
3. Memish ZA, Arabi YM, Ahmed QA, Shibl AM, Niederman MS, GCC CAP Working Group. *et al.* Executive summary of the gulf cooperation council practice guidelines for the management of community-acquired pneumonia. J Chemother 2007;19 Suppl 1:7-11.

4. Memish ZA, Arabi YM, Ahmed QA, Shibl AM, Niederman MS, GCC CAP Working Group. *et al.* Management and prevention strategies for community-acquired pneumonia in the gulf corporation council. J Chemother 2007;19 Suppl 1:33-46.
5. Eldaboosy SA, Halima KM, Shaarawy AT, Kanany HM, Elgamal EM, El-Gendi AA, *et al*. Comparison between CURB-65, PSI, and SIPF scores as predictors of ICU admission and mortality in community-acquired pneumonia. Egypt J Crit Care Med 2015;3:37-44.
6. Al-Tawfiq JA, Diamond M, Joy D, Hinedi K. Performance of CURB-65 in predicting mortality of patients with community-acquired pneumonia in Saudi Arabia. J Infect Dev Ctries 2017;11:811-4.
7. Mahboub B, Al Zaabi A, Al Ali OM, Ahmed R, Niederman MS, El-Bishbishi R, *et al.* Real life management of community-acquired pneumonia in adults in the gulf region and comparison with practice guidelines: A prospective study. BMC Pulm Med 2015;15:112.
8. Al-Abri SS, Al-Maashani S, Memish ZA, Beeching NJ. An audit of inpatient management of community-acquired pneumonia in Oman: A comparison with regional clinical guidelines. J Infect Public Health 2012;5:250-6.
9. Al-Tawfiq JA, Hinedi K, Ghandour J, Khairalla H, Musleh S, Ujayli A, *et al.* Middle East respiratory syndrome coronavirus: A case-control study of hospitalized patients. Clin Infect Dis 2014;59:160-5.
10. Erwin BL, Kyle JA, Allen LN. Time to guideline-based empiric antibiotic therapy in the treatment of pneumonia in a community hospital: A retrospective review. J Pharm Pract 2016;29:386-91.
11. Delaney F, Jackson A. An audit of empiric antibiotic choice in the inpatient management of community-acquired pneumonia. Ir Med J 2017;110:545.
12. Rossio R, Franchi C, Ardoino I, Djade CD, Tettamanti M, Pasina L, *et al.* Adherence to antibiotic treatment guidelines and outcomes in the hospitalized elderly with different types of pneumonia. Eur J Intern Med 2015;26:330-7.
13. Matuz M, Bognar J, Hajdu E, Doro P, Bor A, Viola R, *et al.* Treatment of community-acquired pneumonia in adults: Analysis of the national dispensing database. Basic Clin Pharmacol Toxicol 2015;117:330-4.
14. Mukansi M, Chetty A, Feldman C. Adherence to SATS antibiotic recommendations in patients with community acquired pneumonia in Johannesburg, South Africa. J Infect Dev Ctries 2016;10:347-53.
15. Sakamoto Y, Yamauchi Y, Yasunaga H, Takeshima H, Hasegawa W, Jo T, *et al.* Guidelines-concordant empiric antimicrobial therapy and mortality in patients with severe community-acquired pneumonia requiring mechanical ventilation. Respir Investig 2017;55:39-44.
16. Ewig S, de Roux A, Bauer T, García E, Mensa J, Niederman M, *et al.* Validation of predictive rules and indices of severity for community acquired pneumonia. Thorax 2004;59:421-7.
17. Man SY, Lee N, Ip M, Antonio GE, Chau SS, Mak P, *et al.* Prospective comparison of three predictive rules for assessing severity of community-acquired pneumonia in hong kong. Thorax 2007;62:348-53.
18. Chalmers JD. ICU admission and severity assessment in community-acquired pneumonia. Crit Care 2009;13:156.
19. Nie XM, Li YS, Yang ZW, Wang H, Jin SY, Jiao Y, *et al.* Initial empiric antibiotic therapy for community-acquired pneumonia in Chinese hospitals. Clin Microbiol Infect 2018;24:658.e1-658.e6.
20. Tomczyk S, Jain S, Bramley AM, Self WH, Anderson EJ, Trabue C, *et al.* Antibiotic prescribing for adults hospitalized in the etiology of pneumonia in the community study. Open Forum Infect Dis 2017;4:ofx088.
21. Trad MA, Baisch A. Management of community-acquired pneumonia in an Australian regional hospital. Aust J Rural Health 2017;25:120-4.
22. Kotwani A, Kumar S, Swain PK, Suri JC, Gaur SN. Antimicrobial drug prescribing patterns for community-acquired pneumonia in hospitalized patients: A retrospective pilot study from New Delhi, India. Indian J Pharmacol 2015;47:375-82.
23. Lim WS, Woodhead M; British Thoracic Society. British Thoracic Society adult community acquired pneumonia audit 2009/10. Thorax 2011;66:548-9.
24. Neuman MI, Ting SA, Meydani A, Mansbach JM, Camargo CA Jr. National study of antibiotic use in emergency department visits for pneumonia, 1993 through 2008. Acad Emerg Med 2012;19:562-8.
25. Al-Tawfiq JA. Pattern of antibiotic resistance of *Streptococcus pneumoniae* in a hospital in the Eastern Province Of Saudi Arabia. J Chemother 2004;16:259-63.
26. Al-Tawfiq JA. Antibiotic resistance of pediatric isolates of *Streptococcus pneumoniae* in a Saudi Arabian hospital from 1999 to 2004. Med Sci Monit 2006;12:CR471-5.
27. Memish ZA, Balkhy HH, Shibl AM, Barrozo CP, Gray GC. *Streptococcus pneumoniae* in Saudi Arabia: Antibiotic resistance and serotypes of recent clinical isolates. Int J Antimicrob Agents 2004;23:32-8.
28. Viasus D, Vecino-Moreno M, De La Hoz JM, Carratalà J. Antibiotic stewardship in community-acquired pneumonia. Expert Rev Anti Infect Ther 2017;15:351-9.