Journal of Population Therapeutics & Clinical Pharmacology

**Original Article**
DOI: 10.15586/jptcp.v27iSP1.684

# The comparison of the effectiveness of lincocin® and azitro® in the treatment of covid-19-associated pneumonia: A prospective study

Oguz Guvenmez[1], Hüseyin Keskin[2], Burak Ay[3], Suayip Birinci[4], and Muhammed Furkan Kanca[5]

[1]Independent Researcher, Adana, Turkey

[2]Department of Otorhinolaryngology, Tarsus Medical Park Hospital, Mersin, Turkey

[3]Department of Chemistry, Cukurova University, Science and Arts Faculty, Adana, Turkey

[4]Turkish Ministry of Health, Ankara, Turkey

[5]Cukurova University, Medical Faculty, Adana, Turkey

**Corresponding author:** E-mail: oguzguvenmez001@hotmail.com

**Submitted: 16 April 2020. Accepted: 26 April 2020. Published: 3 June 2020.**

## ABSTRACT

The COVID-19 virus has spread rapidly around the world and there are many patients in multiple countries. Great efforts have been made to find effective medications against the COVID-19. This study aims to compare the effectiveness of LINCOCIN® and AZITRO® in the treatment of COVID-19 associated pneumonia. A total of 24 hospitalized patients aged between 30-80 years who were admitted to the Tarsus Medical Park Hospital between February to March 2020 was included in the study. The patients were divided into LINCOCIN® and AZITRO® treatment groups. Bronchoalveolar-lavage PCR results were compared after treatment. The mean age was 58.4±15.4 years in the LINCOCIN® group and 59.1±16.6 years in the AZITRO® group. In the LINCOCIN® group, the rate of males was 66.7% and it was 58.3% in the AZITRO® group. There were no statistical differences in terms of age and gender between the groups. On the 6th day after starting treatment, negative bronchoalveolar PCR result was 83.3% in the LINCOCIN® group and 33.3% in the AZITRO® group. The negative bronchoalveolar PCR proportion was significantly higher in the LINCOCIN® group than in the AZITRO® group. LINCOCIN® usage may be more appropriate in the treatment of COVID-19 associated pneumonia. Further studies with a large sample size should clarify these results.

**Keywords:** *coronavirus, pneumonia, treatment, COVID-19, medication*

J Popul Ther Clin Pharmacol Vol 27(SP1):e5–e10; 3 June 2020.

## INTRODUCTION

The emergence of the new coronavirus (SARS CoV-2, COVID-19) that appeared in Wuhan, China, in December 2019 poses an important and urgent threat to global health. The COVID-19 virus has spread rapidly and there are many cases in multiple countries now.[1] The World Health Organization (WHO) reported the COVID-19 epidemic as a pandemic in March 2020.[2] A recent study reports that approximately 80% of patients show minor symptoms and the mortality rate is 2.3%. However, the mortality rate increases to 8.0% in patients aged between 70 and 79 years and 14.8% in patients aged over 80 years.[3] Therefore, there is an urgent need for effective treatment to reduce the destructive effects of COVID-19.

Symptoms of COVID-19 may vary in infected patients.[4] Some people may not present any symptoms, although the disease is characterized by fever, cough, and shortness of breath. Other symptoms include tiredness, muscle pain, sore throat, runny nose, and diarrhea. Some patients experienced the loss of smell and taste.[4,5] On the contrary, the disease can cause serious medical conditions and can lead to death in some patients. Older people and patients with chronic medical illnesses are at greater risk of complications. These complications may include pneumonia, acute respiratory distress syndrome (ARDS), sepsis, septic shock, and multiple organ failures.[5]

LINCOCIN® contains lincomycin hydrochloride that inhibits bacterial protein synthesis by binding to the 50S subunit of the bacterial ribosomes.[6,7] LINCOCIN® can be used in many infections caused by staphylococci, streptococci, and pneumococci.[6] AZITRO® contains azithromycin monohydrate that also inhibits protein synthesis by binding to the 50S ribosomal subunit.[8] AZITRO® is used in the treatment of middle ear infections, intestinal infections, sexually transmitted infections, strep throat, pneumonia, and malaria.[9]

Significant efforts have been made to find effective medications against COVID-19 pneumonia around the world. However, there is no definitive treatment. This article has been conducted to assess the effectiveness of LINCOCIN® and AZITRO®. In this study, we hypothesize that LINCOCIN® might be more effective than AZITRO® in the treatment of COVID-19-associated pneumonia.

## METHODS

### *Sample and Procedure*

A total of 24 hospitalized patients aged between 30 and 80 years, who were admitted to the Tarsus Medical Park Hospital between February and March 2020, were included in the study. The nature and purpose of the study were explained to all patients and informant consent was obtained. The approval for this study was received from the Turkish Ministry of Health. The approval number was 2020/34.

The inclusion criteria of the patient group were as follows: (1) an age range of 30–80 years, (2) real-time reverse transcription–polymerase chain reaction (real-time RT-PCR) documented SARS-CoV-2 carriage in the bronchoalveolar-lavage fluid, (3) findings of pneumonia in chest computerized tomography (CT) compatible with COVID-19, (4) no need for ventilatory assistance and (5) not using any medications other than LINCOCIN® and AZITRO®. Patients were included in the study 3 days after symptoms onset. Pregnant patients and patients with known allergy to LINCOCIN® and AZITRO® were excluded from the study.

The patients were divided into LINCOCIN® and AZITRO® treatment groups, respectively. Patients were randomly assigned following simple randomization procedures (computerized

random numbers) to one of two treatment groups. In the first group, the patients received intravenous LINCOCIN® 600 mg twice a day for 5 days. In the second group, the patients received oral AZITRO® 500 mg for the first day and 250 mg for days 2–5. We applied this treatment protocol because the protocol has been reported in previous studies.[10] On the 6th day after starting treatment, PCR findings were compared.

***Coronavirus Detection***

All suspected patients were detected using real-time RT-PCR and those who were positive for the COVID-19 RNA were included in the study. The bronchoalveolar-lavage fluid of the patients was collected and COVID-19 RNA was detected (nucleic acid extraction using Nuclisens Easy Mag®, Biomerieux and amplification with RealStar SARS CoV-2®, Altona).

***Statistical Analysis***

Data analysis was performed by using Statistical Package for Social Sciences-SPSS for IBM, 21.0 program. Demographic variables and general characteristics of the patients were presented by using descriptive statistics. The distribution of the variables was assessed with the Kolmogorov–Smirnov test. Independent sample *t*-test was used to compare normally distributed parametric variables. The chi-square test was used for the comparison of normally distributed categorical variables. A P-value <0.05 was accepted to be statistically significant.

## RESULTS

The data obtained from 24 hospitalized patients aged between 30 and 80 years. The mean age was 58.4±15.4 years in the LINCOCIN® group and 59.1±16.6 years in the AZITRO® group. In the LINCOCIN® group, the rate of males was 66.7% (N = 8) and the rate of females was 33.3% (N = 4). In the AZITRO® group, the rate of males was 58.3% (N = 7) and the rate of females was 41.7% (N = 5). There were no statistical differences in terms of age and gender between the groups (P > 0.05) (Table 1).

Table 2 shows the proportion of negative bronchoalveolar PCR results in the LINCOCIN® and AZITRO® groups. On the 6th day after starting treatment, negative bronchoalveolar PCR result was 83.3% in the LINCOCIN® group and 33.3% in the AZITRO® group. The negative bronchoalveolar PCR proportion was significantly higher in the LINCOCIN® group than in the AZITRO® group (P < 0.05).

In addition, the clinical outcomes were also better in the LINCOCIN® group like duration of hospitalization, temperature normalization, and radiological progression.

**TABLE 1.** Demographic Variables and Clinical Characteristics of the Sample

| | **LINCOCIN®<br>N = 12<br>Mean ± SD** | **AZITRO®<br>N = 12<br>Mean ± SD** | **P*** |
|---|---|---|---|
| **Age (years)** | 58.4±15.4 | 59.1±16.6 | 0.762 |
| | N (%) | N (%) | P** |
| **Gender** | | | |
| Male | 8 (66.7) | 7 (58.3) | 0.061 |
| Female | 4 (33.3) | 5 (41.7) | 0.053 |

**Independent sample t-test was used. **Chi-square test was used.*

**TABLE 2.** The Proportion of Patients with Virologic Cure (Negative Bronchoalveolar PCR), in COVID-19 Patients Treated with LINCOCIN® and AZITRO®

| Treatment | LINCOCIN® N = 12 N (%) | AZITRO® N = 12 N (%) | P* |
|---|---|---|---|
| Before treatment | 0/12 (100) | 0/12 (100) | 0.012 |
| After treatment (6th day) | 10/12 (83.3) | 4/12 (33.3) | |

**Chi-square test was used.*

## DISCUSSION

### *Findings and Comparisons with Similar Studies*

There are contradictory results in previous studies in terms of COVID-19 treatment. Gautret et al. reported that hydroxychloroquine and azithromycin therapy was associated with reduced viral load in patients with COVID-19.[10] In another article, a Chinese team declared that more than 100 patients with COVID-19 pneumonia demonstrated clinical improvements with chloroquine phosphate treatment.[11] On the contrary, Molina et al. reported positive SARS-CoV2 RNA in nasopharyngeal swabs at days 5–6 after treatment initiation with hydroxychloroquine and azithromycin.[12] In addition, a recent study from China found no difference in virologic clearance at 7 days with or without 5 days of hydroxychloroquine. The study also reported no difference in clinical outcomes.[13]

We show here that LINCOCIN® is more effective in clearing viral bronchoalveolar carriage of SARS-CoV-2 in patients with COVID-19 pneumonia. An important difference was observed between LINCOCIN®-treated and AZITRO®-treated patients on the 6th day after treatment initiation. Also, clinical improvements were more prominent in LINCOCIN®-treated patients. This result is of great importance because there is no definitive treatment of COVID-19 pneumonia.

### *Clinical Implications*

The viricidal effects of chloride and alcohol have been demonstrated in many studies.[14–18] LINCOCIN® contains lincomycin hydrochloride, and benzyl alcohol as a preservative.[6] We think that hydrochloride and benzyl alcohol may be responsible for the antiviral effect of LINCOCIN®. Furthermore, lincomycin can also prevent secondary bacterial infections. In this context, LINCOCIN® can be an effective medication in the treatment of COVID-19 pneumonia.

LINCOCIN® can be initiated after positive SARS-CoV-2 carriage in the bronchoalveolar-lavage fluid. On the contrary, a combination with other drugs like antivirals, hydroxychloroquine, or low molecular weight heparin may also be applied.

### *Strengths, Limitations, and Future Directions*

In the present study, we primarily examine the effectiveness of LINCOCIN® and AZITRO® in the treatment of COVID-19-associated pneumonia. According to the results of this study, LINCOCIN® was more effective than AZITRO®. The literature is very limited to this subject and this study can make a significant contribution to the literature.

There are some limitations to the current study. First, the sample size is relatively small. Future studies with a large sample size should be necessary to clarify the findings. Second, the study only focusses on the effectiveness of LINCOCIN® and AZITRO®. The addition of other medications like antiviral agents would improve the quality of the study.

J Popul Ther Clin Pharmacol Vol 27(SP1):e5–e10; 3 June 2020.

***Authors' Contributions***

OG was responsible for the concept and design of the study, analysis and interpretation of data, drafting of the article, and final approval of the version to be published. HK was responsible for acquisition of data, drafting of the article, and final approval of the version to be published. SB was responsible for acquisition of data, drafting of the article and final approval of the version to be published. BA was responsible for analysis and interpretation of data, revising the article critically for important intellectual content, and final approval of the version to be published. MFK was responsible for concept and design, revising the article critically for important intellectual content, and final approval of the version to be published.

## CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest.

## FUNDING

The authors declare that there is no financial support for this article.

## DATA AVAILABILITY STATEMENT

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

## COMPLIANCE WITH ETHICAL STANDARDS

This research was carried out in accordance with the Declaration of Helsinki; the nature and purpose of the study were explained to all patients, and informant consent was obtained in all cases. The Ethics Committee of Adana City Hospital approved the study protocol.

## REFERENCES

1. Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. Int J Antimicrob Agents. 2020;55(3):105924. https://doi.org/10.1016/j.ijantimicag.2020.105924
2. Wang L, Wang Y, Ye D, Liu Q. A review of the 2019 Novel Coronavirus (COVID-19) based on current evidence. Int J Antimicrob Agents. 2020:105948. https://doi.org/10.1016/j.ijantimicag.2020.105948
3. Wu Z, McGoogan JM. Characteristics of and important lessons from the Coronavirus Disease 2019 (COVID-19) outbreak in China: Summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. JAMA – J Am Med Assoc. 2020;323(13):1239–42. https://doi.org/10.1001/jama.2020.2648
4. Wan S, Xiang Y, Fang W, et al. Clinical features and treatment of COVID-19 patients in Northeast Chongqing. J Med Virol. 2020. https://doi.org/10.1002/jmv.25783 [Online ahead of print]
5. Hassan SA, Sheikh FN, Jamal S, Ezeh JK, Akhtar A. Coronavirus (COVID-19): A review of clinical features, diagnosis, and treatment. Cureus. 2020;12(3):e7355. https://doi.org/10.7759/cureus.7355
6. LINCOCIN® (lincomycin HCl) | Pfizer Medical Information – US [Internet]. [cited 2020 Apr 10]. Available from: https://www.pfizermedicalinformation.com/en-us/lincocin
7. Lincocin – FDA prescribing information, side effects and uses [Internet]. [cited 2020 Apr 10]. Available from: https://www.drugs.com/pro/lincocin.html
8. Azithromycin (Systemic) (Professional Patient Advice) – Drugs.com [Internet]. [cited 2020 Apr 10]. Available from: https://www.drugs.com/ppa/azithromycin-systemic.html
9. Azithromycin – Wikipedia [Internet]. [cited 2020 Apr 10]. Available from: https://en.wikipedia.org/wiki/Azithromycin
10. Gautret P, Lagier J-C, Parola P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. Int J Antimicrob Agents. 2020:105949. https://doi.org/10.1016/j.ijantimicag.2020.105949
11. Gao J, Tian Z, Yang X. Breakthrough: Chloroquine phosphate has shown apparent efficacy in

treatment of COVID-19 associated pneumonia in clinical studies. Biosci Trends. 2020;14(1):72–3. https://doi.org/10.5582/bst.2020.01047

12. Molina JM, Delaugerre C, Goff J Le, et al. No evidence of rapid antiviral clearance or clinical benefit with the combination of hydroxychloroquine and azithromycin in patients with severe COVID-19 infection. Médecine Mal Infect. 2020;50(4):384. https://doi.org/10.1016/j.medmal.2020.03.006
13. Chen J, Liu D, Liu L, et al. A pilot study of hydroxychloroquine in treatment of patients with common coronavirus disease-19 (COVID-19). J Zhejiang Univ (Med Sci). 2020;49(February):1–10. https://doi.org/10.3785/j.issn.1008-9292.2020.03.03
14. Li JW, Xin ZT, Wang XW, Zheng JL, Chao FH. Mechanisms of inactivation of hepatitis a virus in water by chlorine dioxide. Water Res. 2004;38(6):1514–19. https://doi.org/10.1016/j.watres.2003.12.021
15. Engelbrecht RS, Weber MJ, Salter BL, Schmidt CA. Comparative inactivation of viruses by chlorine. Appl Environ Microbiol. 1980;40(2):249–56. https://doi.org/10.1128/aem.40.2.249-256.1980
16. Morokutti-Kurz M, Graf C, Prieschl-Grassauer E. Amylmetacresol/2,4-dichlorobenzyl alcohol, hexylresorcinol, or carrageenan lozenges as active treatments for sore throat. Int J Gen Med. 2017;10:53–60. https://doi.org/10.2147/IJGM.S120665
17. Oxford JS, Lambkin R, Gibb I, Balasingam S, Chan C, Catchpole A. A throat lozenge containing amyl meta cresol and dichlorobenzyl alcohol has a direct virucidal effect on respiratory syncytial virus, influenza A and SARS-CoV. Antivir Chem Chemother. 2005;16(2):129–34. https://doi.org/10.1177/095632020501600205
18. Rabenau HF, Kampf G, Cinatl J, Doerr HW. Efficacy of various disinfectants against SARS coronavirus. J Hosp Infect. 2005;61(2):107–11. https://doi.org/10.1016/j.jhin.2004.12.023