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RESEARCH ARTICLE

COMPARISON OF EMPIRICAL ANTIBIOTICS IN COVID19 PNEUMONIA

Onur BAYRAKÇI^{1,*} and Halim BAYRAM²

¹Ersin Arslan Training and Research Hospital, Thoracic Surgery Department

²Ersin Arslan Training and Research Hospital, Infectious Diseases Department

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*Corresponding author:
Onur BAYRAKÇI

ABSTRACT

Covid-19 disease is a fatal viral respiratory disease caused by the SARS-CoV-2 virus. A wide range of clinical findings are seen, from asymptomatic to death. Therefore, it has been observed that empirical antibiotics were frequently used in hospitalizations due to secondary coinfection concerns. The data of 1186 hospitalized patients were analyzed retrospectively. 4 groups (30 patients per group) consisting of a total of 120 patients were formed homogeneously. All patients who fulfilled the criteria (Covid PCR test positive, diagnosed with pneumonia, treated with Favipiravir, normal white blood cell and neutrophil, didn't have bacterial infection, didn't receive anti-inflammatory and steroid-derived drug) were included in the study. Data of all patients (age, gender, comorbidity, laboratory parameters, tomography reports, antibiotic and other drugs, need for intensive care and mortality) were evaluated retrospectively. The first group was levofloxacin, the second group combination of levofloxacin and ceftriaxone, the third group combination of levofloxacin and piperacillin tazobactam, and the fourth group combination of levofloxacin and meropenem. Combination treatment with levofloxacin ceftriaxone and levofloxacin meropenem is more effective in patients with comorbidities. Levofloxacin meropenem or levofloxacin ceftriaxone treatment in patients with interstitial pneumonia and levofloxacin or levofloxacin piperacillin tazobactam treatment in patients with lobular pneumonia is more effective. Levofloxacin ceftriaxone treatment is more effective on the decrease in CRP value, but there is no statistically significant difference between all treatments ($p < 0.05$). Levofloxacin decreases hospital stay more than levofloxacin meropenem. Levofloxacin ceftriaxone decrease hospital stay more than levofloxacin piperacillin tazobactam and levofloxacin meropenem ($p < 0.05$). There is no statistically significant difference between levofloxacin and levofloxacin ceftriaxone as length of hospital stay. Treatment cost sare have been found as levofloxacin < levofloxacin ceftriaxone < levofloxacin piperacillin tazobactam < levofloxacin meropenem.

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INTRODUCTION

Covid 19 is a fatal disease caused by the SARS-CoV-2 virus from the Coronavirus family and declared as a pandemic by the World Health Organization (WHO). Individuals of all ages are at risk of contracting this disease. The risk is more significant in patients aged 60 and over, those with comorbidities (cardiovascular disease, chronic lung disease, obesity, chronic kidney disease, cancer, diabetes mellitus, hypertension), male gender, and smokers [1]. Because it primarily targets the respiratory system, Covid-19 is primarily recognized as a viral respiratory disease. It has been reported that the rate of community-onset bacterial coinfection in these patients is 3.2-3.5%, and this rate increases to 6.1% after

hospitalization [2,3]. It has been observed that empirical antibiotics are frequently used in hospitalized patients due to the fear of secondary coinfection and Covid-19 disease in which clinical findings are detected in a broad spectrum ranging from asymptomatic patients, pneumonia, ARDS and death. For this reason, it was investigated retrospectively, aiming to compare the effects and efficacy of empirical antibiotics on infection parameters.

MATERIALS AND METHODS

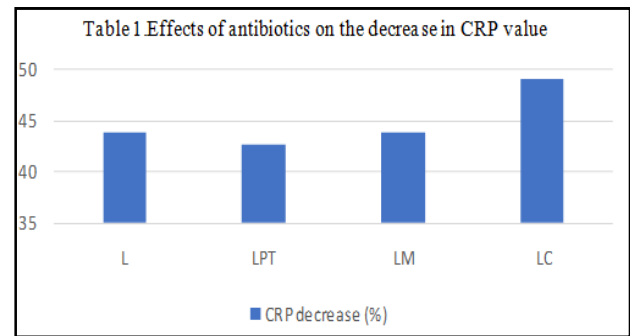
The research has been effectuated in the Ersin Arslan Training and Research Hospital Pandemic Service. The data of 1186 patients hospitalized have been analyzed retrospectively. 4

groups with a total of 120 patients (30 patients per group) have been generated homogeneously. All patients have been positive for Covid PCR test, diagnosed with pneumonia, Favipiravir gotten treatment but did not gotten Hydroxychloroquine. Data of all patients (age, gender, comorbidity, laboratory parameters, tomography reports, antibiotic and drugs gotten, intensive care required, and mortality) have been evaluated. Who did not have pneumonia, had high WBC (White Blood Cells), required antibiotic change, had bacterial infection, got treatment anti-inflammatory and steroid derivative drugs, had no positive Covid PCR test, and in intensive-care patients were not included in the study. The first group levofloxacin, the second group levofloxacin and ceftriaxone combination, the third group levofloxacin and piperacillin tazobactam combination, the fourth group levofloxacin and meropenem combination have been given antibiotic treatments. The laboratory and clinical improvement have been referenced. The homogeneity of the groups have been done by Kolmogorov Smirnov test and statistical analysis SPSS (Statistical Package for the Social Sciences).

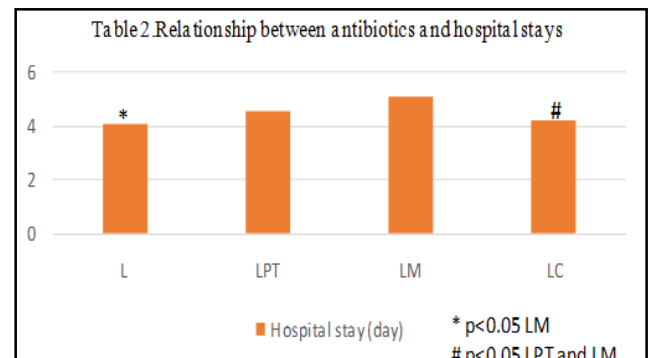
RESULTS

In our study, all patients have been medicated Favipiravir 200 mg (8 g / 5 days) treatment but not hydroxychloroquine. WBC is in the standard range and no lymphopenia. They haven't been gotten any steroid derivatives or anti-inflammatory drugs. The success in the treatment following of the patients has been taken reference decrease in the CRP (C-Reactive Protein) value. Group levofloxacin (L); 14 were female (46,6%) and 16 male (54,4%). Average age was 58.8 (median:62.5, range:24-86). 20 patients had comorbidity, and 10 patients had no comorbidity. Computed tomography (CT) presented signs of bilateral pneumonia (5 interstitial, 19 lobular, 2 lobar, 4 unknew). WBC mean value was 7.6 (median:7.6, range:4.4-10.8). The initial CRP mean value was 59.4 (median: 41.6, range:6.9-256.8). After 500 mg/day levofloxacin treatment, the mean CRP value on day 3 was 32.7 (median:16.9, range:3.5-127.7). CRP value decrease rate was mean 43.8% (median:43.4%, range:9.3%-86%). The average length of stay in the hospital was 4.1 days (median:4, range:3-8) and no death. Group levofloxacin and piperacillin tazobactam combination (LPT); 9 were female (30%) and 21 male (70%). Average age was 60.6 (median:61, range:31-89). 14 patients had comorbidity, and 16 patients had no comorbidity. CT presented signs of bilateral pneumonia (8 interstitials, 20 lobular, 2 unknew). WBC mean value was 7.1 (median:6.8, range:3.7-10.9). The initial CRP mean value was 102.4 (median:89.4, range:12-235). After 500 mg/day levofloxacin and 3x4.5 g/day piperacillin tazobactam combination treatment, the mean CRP value on day 3 was 59 (median:52.6, range:6.2 -147.7). CRP value decrease rate was mean 42.6% (median:45.8%, range:6%-85.7%). The average length of stay in the hospital was 4.6 days (median:4.5, range:3-8) and no death.

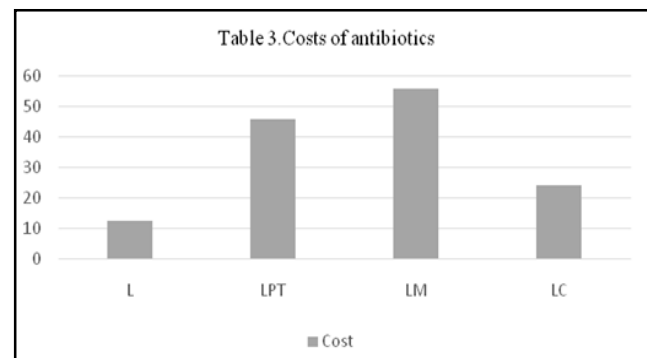
Group levofloxacin and meropenem combination (LM); 10 were female (33.3%) and 20 male (66.7%). Average age was 61.5 (median:63, range:19-82). 18 patients had comorbidity, and 12 patients had no comorbidity. CT presented signs of bilateral pneumonia (12 interstitial, 12 lobular, 1 lobar, 5 unknew). WBC mean value was 8.5 (median: 8.5, range:4.2-10.9).



L:Levofloxacin, LPT:Levofloxacin and Piperacillin tazobactam
LM:Levofloxacin and Meropenem, LC:Levofloxacin and Ceftriaxone



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L:Levofloxacin, LPT:Levofloxacin and Piperacillin tazobactam
LM:Levofloxacin and Meropenem, LC:Levofloxacin and Ceftriaxone

The initial CRP mean value was 131.9 (median:141.5, range:13-261). After 500 mg/day levofloxacin and 3x1 g/day meropenem combination treatment, the mean CRP value on day 3 was 73.8 (median:76.1, range:3.9-204). CRP value decrease rate was mean 43.9% (median:43.9%, range:19.9%-78.7%). The average length of stay in the hospital was 5.1 days (median:5, range:3-8) and no death. Group levofloxacin and ceftriaxone combination (LC); 16 were female (53.3%) and 14 male (46.7%).

Average age was 60.2 (median: 62.5, range:32-83). 19 patients had comorbidity, and 11 patients had no comorbidity. CT presented signs of bilateral pneumonia (11 interstitial, 14 lobular, 1 lobar, 4 unknew). WBC mean value was 6.6 (median:6.6, range:3.9-10.9). The initial CRP mean value was 72.8 (median:49.1, range:12.7-225). After 500 mg/day levofloxacin and 2x1 g/day ceftriaxone combination treatment, the mean CRP value on day 3 was 39.7 (median:23, range:6-117). CRP value decrease rate was mean 49.2% (median:49.5%, range:10%-82.7%). The average length of stay in the hospital was 4.2 days (median:4, range:3-9) and no death.

DISCUSSION

Covid 19 disease is a multisystemic viral disease encountered in a wide spectrum ranging from asymptomatic, symptomatic, mechanical ventilation requirement, acute respiratory failure, septic shock and multi-organ failure. Respiratory system involvement is mostly encountered in hospitalized patients. It is also a concern for clinicians as it causes fatal consequences during the pandemic process. It is known that there is no definite data about secondary bacterial infections that may develop after hospitalization [4]. As in the rest of the world, we found that many clinicians use common empirical antibiotics in our hospital. It has been observed that levofloxacin was preferred most frequently in the ward after hospitalization, and also piperacillin, tazobactam, meropenem, and ceftriaxone combinations were preferred. It has been observed that levofloxacin, piperacillin tazobactam, meropenem, and vancomycin are used in order of frequency in short-term hospitalizations, and colistin, tigecycline, linezolid, and fosfomicin are used in long-term hospitalizations. Acinetobacter and klebsiella growth have been found most frequently in intensive care units during long-term hospitalizations.

We have been observed that empirical antibiotic preferences of the doctors after the first hospitalization were determined by the patient's age, comorbidity, lung involvement on tomography, respiratory distress and oxygen demand, and the most common CRP value. WBC, neutrophil, lymphocyte and procalcitonin values were within the normal range in all groups. CRP value was the criterion in the selection of empirical antibiotics as a laboratory. Therefore, the effects of all empirical antibiotics used were compared with the amount of CRP reduction. All patients with increased WBC, high neutrophil count, increased procalcitonin, changed antibiotics, and all patients who were treated with an anti-inflammatory drug that reduces CRP and steroids were not included in the study. Although antibiotics are not recommended for generally known viral infections, it is aimed to compare the effects of empirical antibiotics, which have been widely used in the pandemic process due to the concern of secondary bacterial infection, on the reduction of CRP value and these effects. In this study detected the rate of decrease in CRP value in the group administered with levofloxacin 43.8% and mean hospital stay 4.1 days, CRP decrease rate 42.6% and mean hospital stay 4.6 day in the levofloxacin piperacillin tazobactam group, CRP decrease rate 43.9% and mean hospital stay 5.1 days in the group administered levofloxacin meropenem, CRP decrease rate 49.2% and mean hospital stay 4.2 days in the levofloxacin ceftriaxone group.

CONCLUSION

Combination treatment with levofloxacin ceftriaxone and levofloxacin meropenem is more effective in patients with comorbidities. Levofloxacin meropenem or levofloxacin ceftriaxone combination treatment in patients with interstitial pneumonia and levofloxacin or levofloxacin piperacillin tazobactam treatment in patients with lobular pneumonia is more effective. Levofloxacin ceftriaxone combination treatment is more effective on the decrease in CRP value (table 1), but there is no statistically significant difference between all treatments ($p < 0.05$).

Levofloxacin treatment decreases hospital stay more than levofloxacin meropenem treatment. Levofloxacin ceftriaxone combination treatment decrease hospital stay more than levofloxacin piperacillin tazobactam treatment and levofloxacin meropenem ($p < 0.05$). There is no statistically significant difference between levofloxacin and levofloxacin ceftriaxone as length of hospital stay (table 2). Treatment cost share has been found as levofloxacin < levofloxacin ceftriaxone < levofloxacin piperacillin tazobactam < levofloxacin meropenem (table 3).

Conflict of interest: All authors declared that there is no conflict of interest.

Ethical approval: For our study, Republic of Turkey Ministry of Health numbered 2020-12-10T12_42_35 and of Gaziantep University Medical Ethics Committee numbered 2021/75 the approval have been obtained.

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