Original Research Article

The effect of levofloxacin combinations on CRP decrease in SARS CoV-2 pneumonia

ABSTRACT

Objective: Covid 19 pneumonia, caused by the SARS-CoV-2 virus, is a disease with severe damage to the lung.It was reported that in Covid 19, rate of 74% antibiotics were used, and secondary bacterial infections were detected in at least 17.6% of the patients who used antibiotics. In this study, the effects of antibiotics in Covid 19 patients who do not use steroid on CRP decrease were aimed.
Materials and Methods: It was done in Ersin Arslan Training and Research Hospital Covid Wards between January 1, 2020 and December 31, 2020. The study included with positive PCR test, 18 age and more than, had normal WBC value, with pneumonia in CT, and use of steroid were excluded.Patients' age, gender, comorbidity, CRP values in the first 24 hours and the 3rd day, antibiotic use, pathological foci on the lung in CT investigated.Accordingly, a total of 202 patients who compatible criteria were included in the study. Chi Square Test was used in the statistical analysis of the data.
Results: The mean age was 60.2±2.57 (19-89). 53.9% of the patients were male and 46.1% female.There was a history of chronic disease in 54.9% of the patients. Findings of pneumonia in CT were 67.8% multifocal and 32.2% unifocal.Antibiotics used were levofloxacin and combined levofloxacin with piperacillin/tazobactam or meropenem or ceftriaxone. When the 1st and 3rd day CRP values were compared; as L<LT<LM<LC rate of decrease were calculated.
Conclusion: According to this study in Covid 19 pneumonia; the combination of levofloxacin with ceftriaxone or meropenem may be preferred as empiric antibiotics in patients 40 age and younger and had comorbidities.The combination of levofloxacin with piperacillin/ tazobactam may be preferred as an empirical antibiotic in patients with multifocal pneumonia in CT. There is no significant difference with the decrease on CRP value among prophylactic antibiotics.Therefore, levoflaxacin alone should be preferred as a prophylactic antibiotic.

Result of statistical data analysis should be showed in abstract section (result section)

Keywords: *antibiotic, Covid-19, CRP, effect, pneumonia*

1.INTRODUCTION

Covid 19 pneumonia, caused by the SARS-CoV-2 virus, is a disease with severe damage to the lung. It is known that most of the deaths caused by Influenza are related to secondary bacterial infections [1]. For this reason, antibiotic use is preferred in fatal Covid 19 pneumonia. It has been reported that the detection of bacterial products in the blood in COVID-19 pneumonia is related with severity of the disease [2]. As it is known, the use of antibiotics in viral infections is not recommended. However, antibiotic use is preferred in Covid 19 due to weakening of the patient's immune system, comorbidity, severe lung

damage, and the risk of secondary bacterial infection. In this study, it was aimed to investigate the effects of antibiotics preferred by physicians on CRP values.

2. MATERİAL AND METHODS

The study done Ersin Arslan Training and Research Hospital Covid Wards between January 1, 2020 and December 31, 2020. It was included with positive Polymerase Chain Reaction (PCR) test, 18 age and more than, had normal white blood cell (WBC), with pneumonia in Computed Tomography (CT). Those who negative PCT test results, younger than 18 years old, did not use of antibiotic and used of steroids were excluded. Accordingly, a total of 202 patients out of 1384 who compatible criteria were included in the study. The normal value range of C-reactive protein (CRP) 0-5 mg/L and WBC value 4-10 mL was accepted. Chi Square Test was used in the statistical analysis of the data.

In this section need more detailed, including Ethical consideration, Population and sample, Technique for data collecting, etc

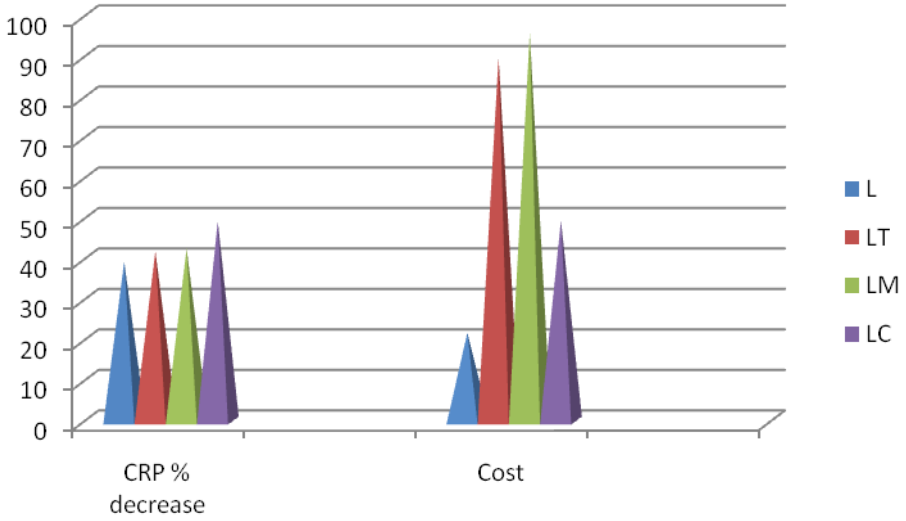
3. RESULTS AND DİSCUSSİON

A total of 202 patients who were compatible with the study criteria were examined. The mean age was 60.2±2.57 (19-89). 53.9% of the patients were male and 46.1% female (table 1). There was a history of chronic disease in 54.9% of the patients. Findings of pneumonia in CT were 67.8% multifocal and 32.2% unifocal. Antibiotics used were levofloxacin (L), levofloxacin combined with piperacillin tazobactam (LT), levofloxacin combined with meropenem (LM), levofloxacin combined with ceftriaxone (LC). Usage doses of antibiotics were L: 500 mg/day, LT: 500 mg + 3x4.5 g / day, LM: 500 mg + 3x1 g / day, LC: 500 mg + 2x1 g /day. CRP values were decrease in all antibiotics used. When the 1st and 3rd day CRP values were compared; L 39.26%, LT 41.88%, LM 42.52%, LC 48.12% rate of decrease were calculated. According to CRP rates of decrease; the order from most to least was LC>LM>LT>L. The cost order of used antibiotics was LM>LT>LD>L (figure 1).

Table 1. distribution of age and gender in the study

		SD	%95 CI
Gender	**n**		
Male	109	0.49	0.08
Female	93		
Age			
Mean	60.2	14.20	2.57

Figure 1. Rates of decrease on CRP and costs in antibiotics



As a result, admitted in wards in patients; Covid 19 pneumonia was more often in male, in over 60 ages and in have a history of chronic disease. LM and LC were preferred more often in the 19-40 age group and with comorbidity (p<0.0001). LT was preferred in multifocal patients according to the pneumonia focus (p<0.07). L and LT were related with a decrease of up to 20% on CRP in multifocal pneumonia (p<0.04). LM and LC were related with a 41-60% decrease on CRP in patients aged 19-40 ages with comorbidity (p<0.01). LC was related 61-80% decrease on CRP in patients with comorbidity (p<0.07). LT and LC were related with more than 80% decrease on CRP in unifocal pneumonia and more than 60 years old (p<0.0001) (table 2). When the 1st and 3rd day CRP values were compared; although there was a decrease on CRP with all antibiotics, there was no statistically significant difference between them (p<0.2, table 3).

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Table 2. Statistical analysis of the study

	N:120	L		LT		LM		LC	
	n	p<	ODSS	p<	ODSS	p<	ODSS	p<	ODSS
Ages (range:19-89)									
19-40	42					0.0001	1.231	0.0001	0.798
41-60	66								
>60	94								
Comorbidity									
Yes	111					0.0001	1.096	0.0001	1.096
No	91								
Involvement of lung									
Unifocal	65								
Multifocal	137	0.06	2.322	0.07	2.786				

CRP decrease (%)									
↓20% and less	35	0.04	1.625	0.03	2.909				
↓21-40%	46								
↓41-60%	64					0.01	1.000	0.01	0.684
↓61-80%	36							0.07	0.982
↓81% and more	21			0.0001	1.000			0.0001	1.000

*L: Levofloxacin LT: Levofloxacin with Piperacillin/Tazobactam LM: Levofloxacin with Meropenem
LC: Levofloxacin with Ceftriaxone

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Table 3. Statistical comparison of the decrease rates of antibiotics on CRP

	L	LT	LM	LC
1st day mean of CRP values	59.40	102.30	131.70	72.80
3st day mean of CRP values	36.08	59.46	75.71	37.77
% decrease of CRP values	**39.26**	**41.88**	**42.52**	**48.12**

*L: Levofloxacin LT: Levofloxacin with Piperacillin/Tazobactam LM: Levofloxacin with Meropenem
LC: Levofloxacin with Ceftriaxone ***p<0.2 Cramer's V:0.984 (Chi Square Test)

The severity of the disease cannot be attributed only to secondary bacterial infections. Because inflammatory cytokine storm is also important in the severity and process of the disease [2]. The high value of procalcitonin, which is used as a biochemical marker in bacterial infection, is related with the severity of the disease in Covid 19 [3]. In Covid 19, high procalcitonin value is seen in many patients. Therefore, the necessity of using antibiotics occurred. Bacterial pneumonias detected early can be effectively treated with antibiotics. Wide spectrum antibiotics are frequently used in Covid 19 patients [4]. In the study, it was observed that levofloxacin and its combinations were frequently preferred as wide-spectrum antibiotics in patients in Covid 19 wards. Although the first WBC values were normal, it was detected levofloxacin combinations were preferred due to the patient's high age (>60) , high CRP value, widespread involvement of lung in CT, and comorbidity. The increase in neutrophil values in the 3rd day may be related to the patient's susceptibility to secondary bacterial infection. Therefore, the related of L, LT, LM and LC with decrease CRP values can be explained by the prevention of secondary bacterial infection. Because the antibiotic used in patients with normal WBC values in Covid 19 is for prophylactic purposes. Effective and rational antibiotic to prefer is essential in pneumonia. Unnecessary use of antibiotics causes an increase in antimicrobial resistance. Resistance to antibiotic is cause for not responding to the treatment, and lack of access to antibiotics kills more people than resistance [5]. In a multicenter study, it was reported that bacterial coinfection was detected at a rate of 9.5% clinically in Covid 19 [6]. In another study; It has been reported that piperacillin/tazobactam, ciprofloxacin, ceftazidime, cefepime, vancomycin, meropenem and cefuroxime are recommended in the treatment of Covid 19 [7]. In this study, levofloxacin, piperacillin tazobactam, meropenem and ceftriaxone were used. Although with the LC combination is decrease on CRP value more , it is not statistically significant (p<0.2). LM is related with less length of hospital stay, but that is no difference with other antibiotics in CRP decreases of rates. Therefore, considering efficacy, cost, and antibiotic resistance, levofloxacin should be used alone as a prophylactic antibiotic. Considering the increase in WBC values in the 3rd day; LC or LM combination can be preferred as empirical antibiotics in patients with comorbidities between 19-40 years of age in Covid 19 pneumonia. In multifocal Covid 19 pneumonia, the LT combination empirically can be preferred. The combination of LT and LC is related with a more than decrease on CRP value. In a study, it was reported that in Covid 19, rate of 74% antibiotics were used, and secondary infections were detected in at least 17.6% of the patients who used antibiotics [8]. Therefore, effective and rational antibiotic

prefer is required in Covid 19 pneumonia. **In discussion section should be support with more references**

4. CONCLUSİON

According to this study in Covid 19 pneumonia; the combination of levofloxacin with ceftriaxone or meropenem may be preferred as empiric antibiotics in patients 40 age and younger and had comorbidities. The combination of levofloxacin with piperacillin tazobactam may be preferred as an empirical antibiotic in patients with multifocal pneumonia in CT. There is no significant difference with the decrease on CRP value among prophylactic antibiotics. Therefore, levoflaxacin alone should be preferred as a prophylactic antibiotic

ETHICAL APPROVAL

Republic of Turkey Ministry of Health 2020-12-10T12_42_35 numbered and Gaziantep University Medical Ethics Committee 2021/75 numbered approval have been received.
COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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Need to add several references for covering the discussion section