Scholars Journal of Medical Case Reports

OPEN ACCESS

Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

Repurposing of Intravenous Piperacillin-Tazobactam in COVID Pneumonitis: A Case Report

Shoebul Haque[1*], Farah Asif [1], Moidur Rehman[2], Abdul Qavi[3]

[1]JR Pharmacology, King George Medical University, Uttar Pradesh, India
[2]Apollo Medics Super Speciality Hospital Lucknow, Uttar Pradesh, India
[3]Department of neurology, RML hospital, Lucknow, Uttar Pradesh, India

DOI: 10.36347/sjmcr.2021.v09i06.007 | **Received:** 03.05.2021 | **Accepted:** 08.06.2021 | **Published:** 13.06.2021

***Corresponding author:** Dr Shoebul Haque

Abstract **Case Report**

Several patients with pneumonia-like symptoms of unknown cause were found linked to the wholesale market in Wuhan, China, in December 2019. The World Health Organization announced on March 11th, 2020, that the outbreak of "Corona Virus Disease 2019" (COVID-19) has become pandemic. At present, we are going through the second wave of infection. To date, no evidence consistently supports any treatment for COVID-19 patients, so identifying new therapeutic options seems beneficial in the management of this disease. This study aimed to report the role of piperacillin-tazobactam antibiotics in patients of COVID-19 disease with bacterial co-infection. In the present case report, the COVID-19 positive patient's clinic-biochemical examination along with HR-CT scan were analyze. Furthermore, along with various symptomatic medications, the role Piperacillin-tazobactam was analyzed after administration. Results show that after administering intravenous piperacillin-tazobactam tothe patient, the patient's general condition improves. The patient's routine blood investigations were to come to normal limits and breaths on normal roomair with SpO2 96%.Based on improvement in patient general condition, oxygen saturation, and in routine blood investigation, we can say that there is some hidden role of intravenous piperacillin-tazobactam injection in the management of COVID-19. Alternatively, we can say that we can decrease the severity of COVID-19 infection by inhibiting the bacterial co-infection. Piperacillin-tazobactam might be useful in the early stages of SARS-CoV-2 infection and the case of bacterial co-infection, although further research is needed to assess the role of piperacillin/ tazobactam in COVID-19 infection.

Keywords: COVID-19, Piperacillin-tazobactam, Empirical therapy, SARS-CoV-2.

INTRODUCTION

A number of patients with pneumonia- like symptoms of unknown cause found linked to the wholesale market in Wuhan, China, in December 2019[1]. Globally, on 18th May 2021, there have been 163,212,543 confirmed cases of COVID-19, including 3,383,979 deaths, reported to WHO. As of 11th May 2021, a total of 1,264,164,553 vaccine doses have been administered[2].

The pathogen which causes COVID-19 is the severe acute respiratory syndrome coronavirus (SARS-CoV-2), a beta coronavirus that is genetically homologous to the SARS coronavirus from the 2003 outbreak (SARS-Co-V)[3]. The World Health Organization (WHO) announced on March 11th 2020, that the outbreak of "Corona Virus Disease 2019" (COVID-19), has become pandemic. On September 4th 2020, the etiologic agent "Severe Acute Respiratory Syndrome (SARS)-CoV-2 spread all over the world[4].

Coronaviruses are enveloped positive-sense single-stranded RNA viruses. SARS-CoV-2 viral particles are spherical to pleomorphic. The viral RNA inside the particle, with 29,811 nucleotides, is tightly coiled and coated by the nucleocapsid (N) protein. Three glycoproteins, called spike (S), membrane (M), and envelope (E), are embedded in the lipid outer membrane [5]. The spike proteins of the Coronaviruses are divided into two domains; S1 and S2. The S1 domain is responsible for receptor binding, while the S2 domain is responsible for cell membrane fusion. In addition, there are eight accessory proteins, four major structural proteins, namely the spike surface glycoprotein (S), a small envelope protein (E), matrix protein (M), and nucleocapsid protein (N). These

structural proteins are positioned in the 3′-terminus of the SARS-CoV-2 genome [6].

RNA viruses are known to have very high rates of mutation and evolution. The high rate of mutation is correlated with virulence modulation and the ability to evolve, which is essential for viral adaptation.

At present, we are going through the second wave of infection, and to date, no evidence consistently supports any treatment for COVID-19patients, so identifying new therapeutic options seems beneficial in the management of this disease.

Case

On 4th May 2021, a 58-year-old man came to the hospital with an 11-day history of high-grade fever, moderate breathlessness, dry cough, lethargy and malaise. At the time of admission on day 11th his blood pressure was 122/86 mm/Hg, heart rate 110/min, and respiratory rate was 22/min. RT-PCR test for covid was positive. His temperature was 100.2 °F, and oxygen saturation was 85% on room air.

HRCT Findings

Patchy ground-glass parenchymal opacities in both lungs- most likely COVID-19 Infection (CT severity score 7/25 mild pulmonary involvement) (Figure-1).

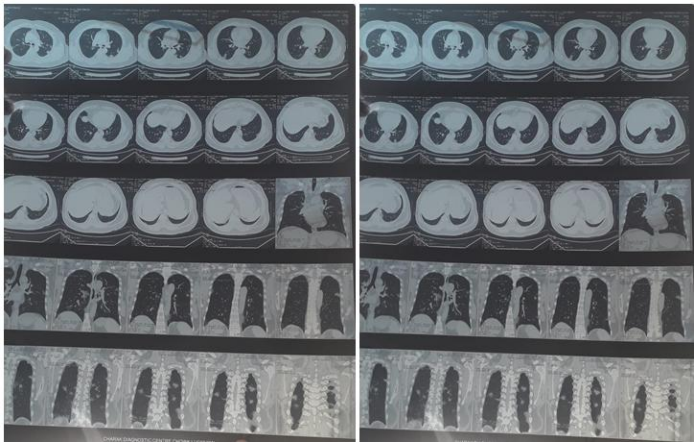

Fig-1: CORADS 5: Finding typical to COVID 19 infection: Patchy ground-glass parenchymal opacities in both lungs- most likely COVID-19 Infection

Past History

Patient having Diabetes Mellitus for last 5 years, patient on oral diabetic medication, no other chronic illnesses were noted.

Present History

Patient having high-grade fever, moderate breathlessness, dry cough, lethargy and malaise from 11 days with SPO2 96% on the first day of symptoms. RT-PCR report of 23rd April revealed positive for COVID-19 -; blood culture report was pending. The patient starts taking oral medications and home oxygen with a venturi mask on 2lit/min on the advice of a local physician, which is described below in (Table 1).

Table-1: Treatment Drugs of the patients

S.no	Drugs	Dose	Freq.	
	Tab. Fabiflu	1800mg on 1st day followed by 800 mg from 2nd to 6th day	Twice a day	6days
	Inj. Ceftriaxone	1gm	12 hourly	5 days
	Tab. Ivermectin	12 mg	Once-daily	5days
	Tab. Azithromycin	500 mg	Once-daily	5 days
	Tab. Doxycycline	100 mg	Two times a day	5 days
	Tab. Dolo	650 mg	Three times a day	5days
	Tab. Limcee	500mg	Two times a day	5days
	Tab. Wyslone	5mg	Two times a day	
	Tab. Pan-D		Two times a day	5days
	Syrup Alex		Three times a day 7.5 ml	5 days
	Nebulization with Duolin & Budecort	snapsules	8 hourly	5days

Laboratory results showed hemoglobin 13.5, TLC- 5,820, platelet count- 1,92,000 DLC count was normal (Table 2).

Table-2: Laboratory results of the patient

Variable	Day 1st results on 24/04/21	Day 5th results on 28/04/21	Normal values
Hemoglobin	13.5	14.1	13.0-17.0
Total leucocyte count	5,820	8000	4000-10,000
Platelet count	1,92,000	1,40,000	1,50,000-4,50,0000
Neutrophils	65 H	81 H	50-62
Lymphocytes	23 L	16 L	25-40
Eosinophils	01	02	01-06
Monocytes	11 H	03	02-08%
Basophils		00	0-1%
E.S.R	08	39 H	0-10
L.D.H	309 H	289 H	135-225
D.Dimer	664.0 H	280.0 H	<500 ng/ml FEU
Ferritin Assay	89.6	301.5 H	13-400
C-reactive Protein	2.11	76.63 H	0-6

After 11 days of medication at home, the patient condition didn't improve, and persistent fever and breathlessness and SpO2 worsened. Also, routine blood investigations didn't show any improvement (table 2, 5th day). On the 11th day, when the patient condition worsened, his family member took him to the hospital and was admitted to the COVID-ward.

On the 2nd day of hospitalization on May 09, 2021, physicians done a routine blood investigation with inflammatory markers, in which leucocyte count was 12,800, neutrophils 86, Lymphocytes 10, C-reactive protein 15.8, Procalcitonin was 0.6. leucocyte counts and inflammatory markers become high.

Table-3: Laboratory results of the patient after hospitalization

Variable	Day 2nd results on hospitalization Day 12th results on 05/05/21	Normal values
Hemoglobin	15.8	13.0-17.0
Total leucocyte count	12,800 H	4000-10,000
Platelet count	1,93,000	1,50,000-4,50,0000
Neutrophils	86 H	50-75
Lymphocytes	10 L	25-40
Eosinophils	03	01-06
Monocytes	01	02-08
Basophils	00	0-1
L.D.H	1102.7 H	135-225
D.Dimer	1.23	0-6
C-reactive Protein	15.8	0-6
Fibrinogen	494 H	150-400
Procalcitonin	0.6 H	0.02-0.3

Based on RT-PCR result, CORADS score, and physicians of the hospital started the empirical therapy with piperacillin-tazobactam intravenous injection 4.5 gm 8hourly (as the patient was already taken Inj. Ceftriaxone i/v 1 gm), was initiated in accordance and oxygen through venturi-mask at 3lit/min started. Symptomatic oral medications and nebulization with budecort-duolin respule 8 hourly started as given below in Table-4.

Table-4: Symptomatic oral medications and nebulization with budecort-duolin of patients

S.no	Drug	Dose	Freq.
1.	Inj Pipzo	4.5 gm i/v	Three times a day
2.	Inj Clexane	0.4 ml s/c	Once daily
3.	Tab Zincovit	50 mg	Twice daily
4.	Tab Dolo	650 mg	Twice daily
5.	Tab Limcee	500mg	Twice daily
6.	Tab omnacortil	5 mg	Twice daily
7.	Tab Pan-D		Twice daily
8.	Syrup Rapitus-Plus	7.5 ml	Three times a day
9.	Nebulization with Duolin & Budecort	1 snapsules	8 hourly

(PIPZO = piperacillin-tazobactam, clexane = enoxaparin, dolo = paracetamol, omnacortil = methylprednisolone, limcee = vitamin C, Duolin = levosalbutamol + ipratropium bromide, budecort = budesonide)

The patient reported initial improvement on May 7th (day 4 of hospitalization); fever subsided, and patient oxygen saturation improved up to 92% on room air. Patients' blood culture report also received by a patient family member in which patient was susceptible to piperacillin/tazobactam, imipenem and cefoperazone/tazobactam otherwise resistant to most of the antibiotics.

On day 7 of hospitalization (May 14, 2021), a repeat routine sample with inflammatory makers was sent for investigation as the patient condition was stable, his SpO2 on normal room air is 96%, and no complaints of fever and breathlessness was there.

As we can see from the results of routine blood investigation, the number of total leucocytes decreases up to 10,300, C-reactive protein is 4.2, d-dimer and procalcitonin level are normal (Table:5). RT-PCR report of the patient is negative.

Table-5: Laboratory results after hospitalization.

Variable	Day 2nd results of hospitalization Day 12th results on 05/05/21	Day 7th results of hospitalization Day 21st results on 14/05/21	Normal values
Hemoglobin	15.8	14.2	13.0-17.0
Total leucocyte count	12,800 H	10,300	4000-10,000
Platelet count	1,93,000	1,46,000	1,50,000-4,50,0000
Neutrophils	86 H	81 H	50-75
Lymphocytes	10 L	10 L	25-40
Eosinophils	03	04	01-06
Monocytes	01	03	02-08
Basophils	00	00	0-1
L.D.H	1102.7 H		135-225
D.Dimer	1.23	0.29	0-6
C-reactive Protein	15.8	4.2	0-6
Fibrinogen	494 H	392	150-400
Procalcitonin	0.6 H	0.2	0.02-0.3

DISCUSSION

Currently, there is no confirmed treatment strategy against COVID-19. Due to the urgency during the second wave of COVID-19-, drug repurposing is widely accepted as the fastest way to identify possible effective therapeutic options[7].

After receiving the blood culture report, it was clear that the physician started empirical therapy, which was the correct decision. As no other option were available and we know that COVID-19 is a life-threatening condition.

Piperacillin-tazobactam is an intravenous antibiotic. Combination of penicillin and b-lactamase inhibitor product that is preferentially prescribed in the hospital or critical care setting for the treatment of moderate to severe infections including hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP), healthcare-associated pneumonia (HCAP), community-acquired pneumonia (CAP) Piperacillin-tazobactam has the broadest spectrum of activity among the penicillin class of b-lactam antibiotics and is generally active against most of the typical human pathogens including aerobic and anaerobic Gram-positive and Gram-negative bacteria[8].

Piperacillin-tazobactam might be useful in the early stages of SARS-CoV-2 infection and in the case of bacterial co-infection, further research is needed to access the role of piperacillin/tazobactam in COVID-19 infection. Based on improvement in patient general condition, oxygen saturation and routine blood investigation, we can say that there is some hidden role of intravenous piperacillin-tazobactam injection in the management of COVID-19. Alternatively, we can say that we can decrease the severity of COVID infection by inhibiting the bacterial co-infection.

However, enlightening the relevance of any therapeutic intervention from a single case report is always controversial since clinical outcomes may be influenced by some confounding factors such as the concomitant use of other therapies. But we believe that intravenous piperacillin-tazobactam should be considered a beneficial treatment for COVID-19.

Funding

No external funding was received.

Declaration of Competing Interest

Shoebul Haque is the principal investigator of a non-sponsored randomized trial assessing the therapeutic role of intravenous piperacillin-tazobactam in COVID-19 patients. The rest of the authors are sub-

investigators in this project. All authors declare no other competing interests.

REFERENCES

1. Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J. (2020). A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med, 382(8); 727–33.
2. WHO Coronavirus Disease (COVID-19) Dashboard|WHO Coronavirus Disease (COVID-19) Dashboard. Who.int.
3. Wang, J., Peng, Y., Xu, H., Cui, Z., Williams, R.O. (2020). The COVID-19 Vaccine Race: Challenges and Opportunities in Vaccine Formulation. AAPS PharmSciTech, 21(6); 1–12.
4. Asselah, T., Durantel, D., Pasmant, E., Lau, G., Schinazi, R.F. (2021). COVID-19: Discovery, diagnostics and drug development. J Hepatol [Internet], 74(1);168–84. Available from: https://doi.org/10.1016/j.jhep.2020.09.031
5. Ruiz-Hitzky, E., Darder, M., Wicklein, B., Ruiz-Garcia, C., Martín-Sampedro, R., del Real, G. (2020). Nanotechnology Responses to COVID-19. Adv Healthc Mater, 9(19); 1–26.
6. Jee, H., Nwagwu, C., Anyim, O., Ekweremadu, C., Kim, S. (2020). Since January 2020 Elsevier has created a COVID 19 resource centre with free information in English and Mandarin on the novel coronavirus COVID- 19 . The COVID-19 resource centre is hosted on Elsevier Connect , the company' s public news and information. 2020;(January).
7. Elmezayen, A.D., Al-Obaidi, A., Şahin, A.T., Yelekçi, K. (2020). Drug repurposing for coronavirus (COVID-19): in silico screening of known drugs against coronavirus 3CL hydrolase and protease enzymes. J Biomol Struct Dyn, 1-13.
8. Gin, A., Dilay, L., Karlowsky, J.A., Walkty, A., Rubinstein, E., Zhanel, G.G. (2007). Piperacillin – tazobactam : a β -lactam / β -lactamase inhibitor combination, 365-83.