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CASE REPORT **CORONA EXPERIENCE**

A promising therapy of tocilizumab and helmet CPAP to prevent intubation for COVID-19 induced severe ARDS: a case report

Septian Adi Permana[1*], Adhrie Sugiarto[1], Muhammad Husni Thamrin[2], Arifin[2], Harsini[3]

Author affiliations:

1- Anesthesiology & Intensive Care Department, University Indonesia, Jakarta, Indonesia
2- Intensive Care Department, Dr Moewardi General Hospital, Surakarta, Indonesia
3- Pulmonology Department, Dr Moewardi General Hospital, Surakarta, Indonesia

***Correspondence:** Septian Adi Permana; E-mail: septian.adi03@gmail.com

Abstract

A 59 yrs old male with severe ARDS due to COVID-19 infection was in life threatening 'cytokine storm'. He had also co-morbids including diabetes mellitus and hypertension. He had come from Grobogan, a red area for COVID-19. Clinical finding indicted systemic inflammatory response syndrome (SIRS) with dyspnea, tachycardia, and high fever. Laboratory tests showed raised leukocyte count, CRP, SGOT/SGPT, blood sugar, PCT, low PaO_2/FiO_2 ratio. RT PCR showed he was infected by COVID-19. Sputum culture showed Klebsiella infection and CXR showed bilateral pneumonia.

Patient was treated with standard therapy and a combination of tocilizumab for cytokine-storm and helmet CPAP for severe ARDS.

Helmet CPAP has become the first modality for COVID-19 ARDS in some countries but not in Indonesia. We chose helmet CPAP because of the cost efficient, comfortable, and easy operation compared to other modality. We chose tocilizumab because it uses a single dose. Although it is expensive, only one dose is enough and it is effective in blocking the cytokine storm. We found that helmet CPAP and tocilizumab combination in COVID-19 lead severe ARDS could be promising to prevent intubation for patients.

Key words: Helmet CPAP; ARDS; COVID-19; Tocilizumab; Cytokine storm

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1. Introduction

We present a case of a severe ARDS due to COVID-19 infection and a "cytokine-storm", which was diagnosed by the clinical signs; he had systemic inflammatory response syndrome (SIRS), and from the laboratory reports (high CRP).[1] In ARDS, the PaO_2 / FiO_2 ratio is deranged. From Berlin's criteria, we can classify ARDS. For the ARDS management we use flowchart from recent guidelines for management of ARDS in COVID-19, most of which prefer using non-invasive technique initially. One of the techniques is helmet CPAP.[2-7]

Helmet CPAP is a device delivering positive pressure without invasive methods and it is more comfortable than mask. It is stable, allow longer use and has less complications than the mask.[4] To minimize complications such as CO_2 entrapment and noise, we use a moderate flow of 45 l/min and use HME filter to create warm and humid air and to reduce noise.[3, 5] From a recent study published in Italy, a combination of helmet CPAP and prone position seems to be promising to prevent intubation in COVID-19 induced

ARDS patient and become the first choice for ARDS induced by COVID-19 in Italy.[4, 6] Helmet CPAP cannot decrease the work of breathing actively, but by recruiting the alveoli, it improves compliance, and normalizes the ventilation perfusion mismatch in ARDS induced by COVID-19.[6, 7] The use of helmet CPAP has been proven to recruite non-aerated alveoli in dependent pulmonary regions, it also helps to stabilize the airways. Moreover, CT scan showed that helmet CPAP produces homogeneity of distribution in the lung volume.[7]

The use of tocilizumab has been recommended by a recent study, which included 250 patients with COVID-19 in four different countries, and showed that the use of tocilizumab can improve clinical condition and lower the mortality; even though the benefit was not statistically significant in some other studies.[8-11] This therapy is safe and effective for COVID-19 patients even with mild and moderate renal insufficiency.[8, 11] This drug improves clinical condition within 12 to 72 hours, which continues to improve over the next ten days. Tocilizumab work in blocking iL-6 receptor that can improve the "cytokine-storm" state.[11] Some researchers have suggested to make this drug as a rescue therapy.[9, 10]

2. Case report

A 52 yrs old male, positive for covid-19 in rapid test, presented with fever, dyspnea and tachycardia. The patient had no history of dyspnea before the current illness. He was on treatment for diabetes mellitus and hypertension. He lived in an area which is endemic for COVID-19.

2.1. Clinical features

His clinical examination revealed body temperature 39.4°C, respiratory rate 28-32/min, pulse rate 129 bpm, and blood pressure 139/64 mmHg. On chest examination, we found ronchi in both sides of the chest. Laboratory findings showed leukocytosis (11,890/mm^3), high blood sugar (323 mg/dl), high CRP (26 mg/l), low serum sodium (126 mmol/l), low chloride (91 mmol/l), high SGOT (355 u/l), high SGPT (156 u/l), and high procalcitonin (4.19 ng/ml). From the rapid test of antibodies IgM and IgG for COVID-19 was reactive. Other laboratory findings (hemoglobin, platelets, bilirubin, urea and creatinine)

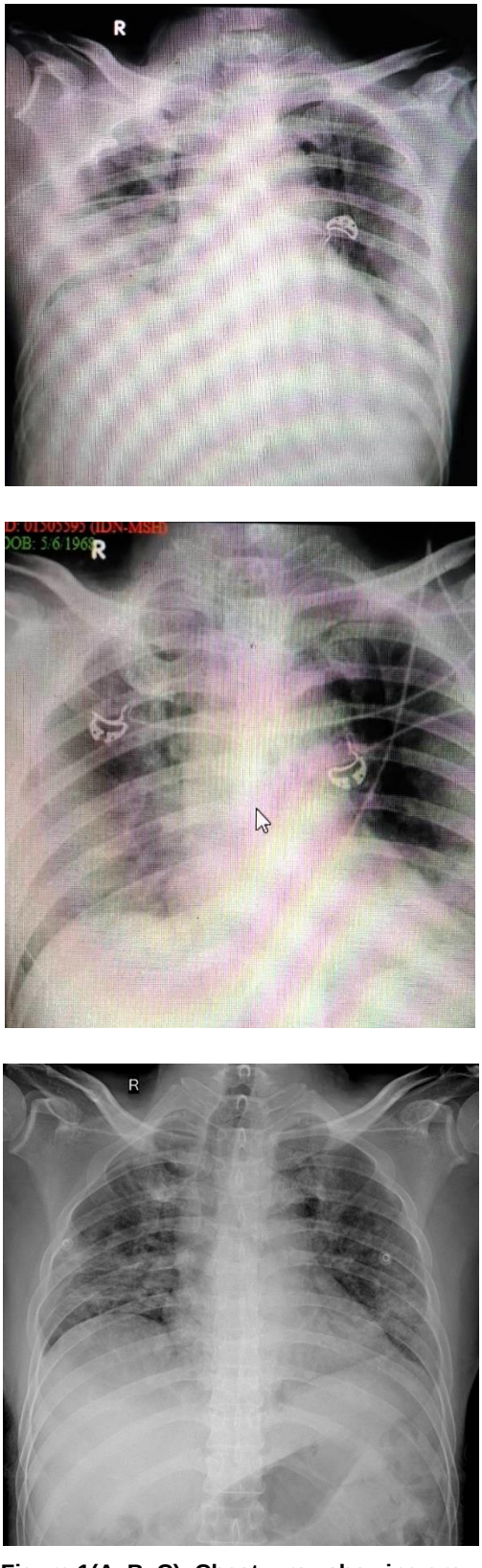

Figure 1(A, B, C): Chest x-ray showing gra dual improvement in lung structure

were normal. His chest x-ray showed signs of pneumonia suspected of COVID-19 (Figure 1). On day 3, his SpO_2 fell low (88-92%) with increase in supplemental O_2, using non-rebreather mask (NRM) up to 12-15 l/min, D-dimer level was 6922 ng/ml. So he was transferred to ICU.

2.2. Timeline

Table 1: Vital signs and therapy

Day	1	2	3		4	5	15	17	18	19	25
			pre	post							
GCS	CM	CM	CM	CM	CM	CM	CM	CM	CM	CM	CM
BP (mmHg)	139 / 64	124 / 82	124 / 98	110 / 96	129 / 97	155 / 109	141 / 105	141 / 105	124 / 82	155 / 109	135 / 73
HR (bpm)	129	118	112	77	89	93	89	88	88	87	87
RR (xpm)	28	28	28	22	27	27	26	28	24	24	19
Temp(°C)	39.4	38.8	38.6	36.8	36.8	36.8	36.5	36.5	36.5	36.5	36.5
SpO_2 (%)	96	92	88	100	95	95	99	100	100	100	97
Therapy	NRM 8 l/min	NRM 12 l/min	NRM 12 l/min	Helmet CPAP	NRM 7 l/min	NRM 7 l/min	NRM 7 l/min	NRM 7 l/min	Nasal cannula 5 l/min, prone	Nasal cannula 4-5 l/min	Room air
				Tocilizumab		Convalescent plasma	Swab taken	PCR from swab day 15 negative	Move to ICU non-covid	Move to ward	Discharge home

NRM = non-rebreather mask, CPAP = Continuous positive airway pressure

2.3. Diagnostic Assessment

This patient was diagnosed with severe COVID-19 from real time PCR, severe ARDS from blood gas analysis (PaO_2/FiO_2 ratio 54), and co-infection with bacterial pneumonia (Klebsiella pneumoniae) from sputum culture. His co-morbid diseases were confirmed by laboratory test; diabetes mellitus from high blood sugar test; and hypertension and heart disease from blood pressure and chest x-rays (a cardiothoracic ratio 52%).

Figure 2: Patient with Helmet CPAP

2.4. Therapeutic interventions

The patient in ICU got helmet CPAP for oxygen supplementation. Then for the cytokine storm management, we used tocilizumab 400 mg once combined with dexamethasone 5 mg q8hr. The initial blood and sputum cultures were positive for Klebsiella infection, which was sensitive to piperacillin/tazobactam. We check the D-dimer level, and the result was high (6922 ng/ml), so we started prophylactic anticoagulant. Additional therapies for this patient included;

- Piperacillin/tazobactam 4.5 g q6hr for bacterial infection
- Azithromycin 500 mg q.i.d, as standard covid therapy
- N-acetylcysteine (NAC) 10% 6 ml q.i.d, as mucolytic
- Vitamin C 2 g q8hr as standard covid therapy
- Insulin aspart (Novorapid®) 8-8-8 iu, Insulin glargine (Lantus®) 0-0-0-10 iu for diabetes mellitus

- Enoxaparine 40 mg q12hr, as a prophylactic anticoagulant
- Carvedilol (Coreg®) 3.25 mg q.i.d., for rate control
- Dexamethasone 5 mg q8hr for reducing cytokine storm

2.5. Follow-up and Outcomes

This patient was followed up daily, for vital signs and main symptoms. For laboratory testing we checked blood sugar twice a day. Other laboratory check-up was based upon clinical condition of the patient. To document the benefits of helmet CPAP plus other medication, repeated blood gas analysis and chest x-rays were ordered.

3. Discussion

This patient was in severe ARDS when he was admitted to ICU, and after applying helmet CPAP the SpO_2 increased to 100%. From blood gas analysis his PaO_2 was 167.8 mmHg, with $PaCO_2$ 33.5 mmHg. The $PaCO_2$ is higher when patient using helmet CPAP than when we decrease the O_2 supplementation with NRM 7 l/min. It may be because the RR was decreased when using helmet CPAP. This patient also suffered cytokine storm, which is indicated from the raised CRP and the sign of SIRS, so we administered tocilizumab 400 mg within 90 min. After that, the clinical condition gradually got better, the fever became normal, the HR and blood pressure decreased, and the patient felt more comfortable. The clinical signs showed better steady progress until the patient was discharged home.

Patient felt more comfortable after using helmet CPAP and receiving tocilizumab. The dyspnea got better, breathing became easier, and the fever got settled. After receiving the therapy, he could eat by himself, without the assistance by the nurse. And one day after combination therapy, he could read Quran by himself, he could speak again. Just the day before he had no strength to do it. We conclude that helmet CPAP can be considered in COVID patients with falling oxygen levels, along with high flow nasal oxygenation, BIPAP and conventional CPAP, before intubating the patients.

4. Competing interests

The authors have full access to all the data, take full responsibility for the accuracy of the data, and have authority over manuscript preparation and decisions to submit the manuscript for publication.

5. Authors' contribution

SAP: Concept, Conduct of study, Manuscript writing
AS, MHT: Conduct of study, Manuscript editing
A, H: Conduct of study, References

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