ISSN 2307-8960 (online)

World Journal of *Clinical Cases*

World J Clin Cases 2021 May 16; 9(14): 3227-3486

Published by Baishideng Publishing Group Inc

World Journal of Clinical Cases

Contents

Thrice Monthly Volume 9 Number 14 May 16, 2021

World Journal of Clinical Cases

Thrice Monthly Volume 9 Number 14 May 16, 2021

Contents

World Journal of Clinical Cases

Thrice Monthly Volume 9 Number 14 May 16, 2021

Contents

World Journal of Clinical Cases

Thrice Monthly Volume 9 Number 14 May 16, 2021

Contents

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Nicola Montemurro, MD, PhD, Assistant Professor, Consultant Physician-Scientist, Neurosurgeon, Surgeon, Surgical Oncologist, Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa 56126, Italy. nicola.montemurro@unipi.it

AIMS AND SCOPE

The primary aim of *World Journal of Clinical Cases* (*WJCC*, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

The *WJCC* is now indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, PubMed, and PubMed Central. The 2020 Edition of Journal Citation Reports® cites the 2019 impact factor (IF) for *WJCC* as 1.013; IF without journal self cites: 0.991; Ranking: 120 among 165 journals in medicine, general and internal; and Quartile category: Q3. The *WJCC*'s CiteScore for 2019 is 0.3 and Scopus CiteScore rank 2019: General Medicine is 394/529.

RESPONSIBLE EDITORS FOR THIS ISSUE

NAME OF JOURNAL
World Journal of Clinical Cases

ISSN
ISSN 2307-8960 (online)

LAUNCH DATE
April 16, 2013

FREQUENCY
Thrice Monthly

EDITORS-IN-CHIEF
Dennis A Bloomfield, Sandro Vento, Bao-Gan Peng

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/2307-8960/editorialboard.htm

PUBLICATION DATE
May 16, 2021

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Clinical Cases

Submit a Manuscript: https://www.f6publishing.com

World J Clin Cases 2021 May 16; 9(14): 3385-3393

DOI: 10.12998/wjcc.v9.i14.3385

ISSN 2307-8960 (online)

CASE REPORT

Almitrine for COVID-19 critically ill patients – a vascular therapy for a pulmonary vascular disease: Three case reports

Pierre Huette, Osama Abou Arab, Vincent Jounieaux, Mathieu Guilbart, Mohamed Belhout, Guillaume Haye, Hervé Dupont, Christophe Beyls, Yazine Mahjoub

ORCID number: Pierre Huette 0000-0003-1563-4869; Osama Abou Arab 0000-0003-3766-716X; Vincent Jounieaux 0000-0003-2131-6429; Mathieu Guilbart 0000-0001-9942-1953; Mohamed Belhout 0000-0002-9459-1387; Guillaume Haye 0000-0002-4791-0349; Hervé Dupont 0000-0002-5644-3412; Christophe Beyls 0000-0001-8949-7348; Yazine Mahjoub 0000-0002-5867-146X.

Author contributions: Huette P, Abou Arab O, Beyls C and Mahjoub Y conceived the study and drafted the manuscript; Jounieaux V, Guilbart M, Belhout M, Haye G and Dupont H participated in data acquisition and helped to draft the manuscript.

Informed consent statement: Local institutional review board waived the need for written informed consent; data storage was authorized by national licensing authority (CNIL PI2020_843_0026). Patients and/or next of kin were informed of the study.

Conflict-of-interest statement: The authors declare no conflict of interest.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE

Pierre Huette, Osama Abou Arab, Mathieu Guilbart, Guillaume Haye, Hervé Dupont, Christophe Beyls, Yazine Mahjoub, Department of Anaesthesia and Critical Care, Amiens Hospital University, Amiens 80000, France

Vincent Jounieaux, Department of Respiratory Medicine, Amiens Hospital University, Amiens 80000, France

Mohamed Belhout, Department of Pharmacy, Amiens Hospital University, Amiens 80000, France

Corresponding author: Pierre Huette, MD, Doctor, Department of Anaesthesia and Critical Care, Amiens Hospital University, Avenue Rene-Laennec, Amiens 80000, France. huette.pierre@chu-amiens.fr

Abstract

BACKGROUND

Several reports with clinical, histological and imaging data have observed the involvement of lung vascular function to explain the severe hypoxemia in coronavirus disease 2019 (COVID-19) patients. It has been hypothesized that an increased pulmonary blood flow associated with an impairment of hypoxic pulmonary vasoconstriction is responsible for an intrapulmonary shunt. COVID-19 may lead to refractory hypoxemia (PaO_2/FiO_2 ratio below 100 mmHg) despite mechanical ventilation and prone positioning. We hypothesized that the use of a pulmonary vasoconstrictor may help decrease the shunt and thus enhance oxygenation.

CASE SUMMARY

We report our experience with three patients with refractory hypoxemia treated with almitrine to enhance oxygenation. Low dose almitrine (Vectarion®; Servier, Suresnes, France) was started at an infusion rate of 4 μg × kg/min on a central line. The PaO_2/FiO_2 ratio and total respiratory system compliance during almitrine infusion were measured. For the three patients, the PaO_2/FiO_2 ratio time-course showed a dramatic increase whereas total respiratory system compliance was unchanged. The three patients were discharged from the intensive care unit. The intensive care unit length of stay for patient 1, patient 2 and patient 3 was 30 d, 32 d and 31 d, respectively. Weaning from mechanical ventilation was performed 13 d, 18 d and 15 d after almitrine infusion for patient

Checklist (2016).

Manuscript source: Unsolicited manuscript

Specialty type: Critical care medicine

Country/Territory of origin: France

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

Received: November 17, 2020
Peer-review started: November 17, 2020
First decision: December 28, 2020
Revised: December 31, 2020
Accepted: January 25, 2021
Article in press: January 25, 2021
Published online: May 16, 2021

P-Reviewer: Shahini E
S-Editor: Zhang H
L-Editor: Filipodia
P-Editor: Zhang YL

1, 2 and 3, respectively. We found no deleterious effects on the right ventricular function, which was similar to previous studies on almitrine safety.

CONCLUSION
Almitrine may be effective and safe to enhance oxygenation in coronavirus disease 2019 patients. Further controlled studies are required.

Key Words: COVID-19; Treatment; Acute vascular distress syndrome; Almitrine; Intensive care unit; Safety; Case report

Core Tip: It has been hypothesized that increased pulmonary blood flow associated with impaired hypoxic vasoconstriction may lead to significant intrapulmonary shunt that plays a major role in coronavirus disease 2019 related severe hypoxia. In this report, three coronavirus disease 2019 patients with refractory hypoxemia were treated with continuous infusion of almitrine, a specific pulmonary vasoconstrictor. Almitrine infusion enhanced oxygenation of patients with severe coronavirus disease 2019 related acute respiratory distress syndrome without any change in pulmonary artery pressures and right ventricular function.

Citation: Huette P, Abou Arab O, Jounieaux V, Guilbart M, Belhout M, Haye G, Dupont H, Beyls C, Mahjoub Y. Almitrine for COVID-19 critically ill patients – a vascular therapy for a pulmonary vascular disease: Three case reports. *World J Clin Cases* 2021; 9(14): 3385-3393
URL: https://www.wjgnet.com/2307-8960/full/v9/i14/3385.htm
DOI: https://dx.doi.org/10.12998/wjcc.v9.i14.3385

INTRODUCTION

Several reports with clinical, histological and imaging data in coronavirus disease 2019 (COVID-19) have observed that the involvement of lung vascular function may explain the severe hypoxemia[1-5]. It has been hypothesized that an increased pulmonary blood flow is responsible for an intrapulmonary shunt with a decrease of ventilation/perfusion ratio[2,3]. Recently, three retrospective case series reported the use of almitrine, a pulmonary vasoconstrictor, in COVID-19 patients with inconsistent effects on oxygenation and outcome[6-8]. However, no data on key safety factors, such as right ventricular function or pulmonary artery pressure, were reported in these series. We report our experience with three patients with refractory hypoxemia treated with almitrine to enhance oxygenation. Complete hemodynamic assessment with transesophageal echocardiography and pulmonary artery catheter was performed.

CASE PRESENTATION

Chief complaints

Patients were admitted at Amiens University hospital intensive care unit for severe acute respiratory distress syndrome (ARDS) related to COVID-19. Severe acute respiratory syndrome coronavirus-2 infection was confirmed by real-time reverse transcription polymerase chain reaction on a sample from nasopharyngeal swab. Patient condition deteriorated rapidly leading to mechanical ventilation and refractory hypoxemia despite medical management.

History of present illness

Case 1: The patient was admitted to the hospital 7 d after onset of symptoms (dyspnea and headache). Initial treatment included lopinavir/ritonavir and high flow nasal oxygen for 2 d. Respiratory worsening lead to mechanical ventilation 2 d after hospital admission.

Case 2: The patient was admitted to the hospital 11 d after onset of symptoms (dyspnea and cough). Initial treatment included lopinavir/ritonavir. Respiratory worsening required mechanical ventilation 5 d after intensive care unit (ICU) admission.

Case 3: The patient was admitted to the hospital 5 d after symptoms onset (anosmia, dyspnea and cough). He was admitted to the ICU because of respiratory worsening 6 d after hospital admission. After 5 d with high flow nasal oxygen, respiratory worsening required mechanical ventilation. After 2 d of mechanical ventilation, the patient developed severe ARDS.

History of past illness

The patients' medical histories is presented in Table 1. The first patient was a 57-year-old female with a medical history of smoking and hypertension. The second patient was a 56-year-old female with a medical history of dyslipidemia and obesity (body mass index (BMI) = 39 kg/m^2). The third patient was a 53-year-old male with a history of obesity (BMI = 40 kg/m^2) and rheumatoid arthritis treated with steroids.

Personal and family history

The patients had no personal or family history.

Physical examination

Case 1: Prior to almitrine infusion, the plateau pressure was 28 cmH_2O and positive end expiratory pressure (PEEP) at 14 cmH_2O. Baseline pulmonary compliance was 32 mL/cmH_2O. Pulmonary artery catheter showed pulmonary vascular resistance at 5.9 Wood units and pulmonary artery occlusion pressure of 7 mmHg. Cardiac index (CI) was 2.6 L/min/m^2. Right ventricular (RV) fractional area change (FAC) was 45%. Speckle tracking based right ventricular two-dimensional strain was performed (Table 1 and Figure 1).

Case 2: Prior to almitrine infusion, the plateau pressure was 27 cmH_2O and PEEP at 14 cmH_2O. Baseline pulmonary compliance was 33 mL/cmH_2O. Pulmonary artery catheter showed pulmonary vascular resistance at 4.1 Wood units and pulmonary artery occlusion pressure of 9 mmHg. CI was 2.9 L/min/m^2. RV FAC was 42%.

Case 3: Prior to almitrine infusion, the plateau pressure was 29 cmH_2O and PEEP at 15 cmH_2O. Baseline pulmonary compliance was 31 mL/cmH_2O. Pulmonary artery catheter showed pulmonary vascular resistance at 3.3 Wood units and pulmonary artery occlusion pressure of 11 mmHg. CI was 2.9 L/min/m^2. RV FAC was 58%.

Laboratory examinations

Case 1: Prior to almitrine infusion, the PaO_2/FiO_2 ratio was 77 mmHg. Arterial blood gas sample showed $PaCO_2$ of 46.2 mmHg, pH at 7.4 and lactate at 1.8 mmol/L. Laboratory investigations revealed lymphopenia at 550/mm^3 and high C reactive protein level at 65 mg/L.

Case 2: Prior to almitrine infusion, the PaO_2/FiO_2 ratio was 91 mmHg. Arterial blood gas sample showed $PaCO_2$ of 39.5 mmHg, pH at 7.4 and lactate at 1.9 mmol/L. Laboratory investigations revealed lymphopenia at 370/mm^3 and high C reactive protein level at 95 mg/L.

Case 3: Prior to almitrine infusion, the PaO_2/FiO_2 ratio was 95 mmHg. Arterial blood gas sample showed $PaCO_2$ of 49 mmHg, pH at 7.3 and lactate at 1.4 mmol/L. Laboratory investigations did not reveal any other specificities.

Imaging examinations

Case 1: Chest computed tomography (CT) angiography showed ground-glass opacity with crazy paving and severe lobar involvement (> 75%). There was no pulmonary embolism.

Case 2: Chest CT angiography showed ground-glass opacity with crazy paving and moderate lobar involvement (50%-75%). There was no pulmonary embolism.

Case 3: Chest CT angiography showed ground-glass opacity with bilateral crazy paving, consolidation and limited lobar involvement (25%). There was no pulmonary embolism.

Table 1 Patients' characteristics prior and after almitrine infusion

Variables	Case 1	Case 2	Case 3
Age in yr	57	56	53
BMI in kg/m^2	38.9	39.0	40.1
Gender	Female	Female	Male
Medical history	Smoking, hypertension, obesity	Dyslipidemia, obesity	Rheumatoid arthritis, obesity
Medication use	None	Statin	Steroids
Days from symptom onset to hospital admission in d	7	11	5
Days from hospital admission to ICU admission in d	2	6	6
High flow or low flow oxygen support prior to mechanical ventilation in d	2	5	5
Mechanical ventilation prior to almitrine infusion in d	2	1	2
Chest CT scan	GGO, crazy paving and severe lobar involvement (> 75%), no pulmonary embolism	GGO, crazy paving and moderate lobar involvement (50%-75%), no pulmonary embolism	GGO, bilateral crazy paving, consolidation, limited lobar involvement (25%), no pulmonary embolism
Respiratory management	Two sessions	No	Two sessions
Prone positioning before almitrine infusion/Position during almitrine infusion	Supine	Supine	Supine
Hemodynamic parameters ICU admission			
HR as /min	66	115	61
SAP in mmHg/DAP in mmHg MAP in mmHg	115/50 (71)	119/69 (85)	124/61 (82)
SpO2, %	90	90	
Lactate in mmol/L	1.800	1.900	1.493
Norepinephrine infusion as µg × kg × min^{-1}	0.09	-	0.35
SAPS II	68	40	56
SOFA	13	7	8
Respiratory parameters			
Baseline			
PaO_2/FiO_2	77	91	95
PEEP in cmH_2O	14	14	15
Plateau pressure in cmH_2O	28	27	29
Compliance in mL/cmH_2O	32	33	31
H1			
PaO_2/FiO_2	82	150	121
PEEP in cmH_2O	14	14	15
Plateau pressure in cmH_2O	30	29	28
Compliance in mL/cmH_2O	29	28	33
H2			
PaO_2/FiO_2	163	330	135
PEEP in cmH_2O	14	14	15

Plateau pressure in cmH_2O	30	29	28
Compliance in mL/cmH_2O	28	29	33
H12			
PaO_2/FiO_2	233	160	214
PEEP in cmH_2O	14	14	15
Plateau pressure in cmH_2O	30	27	28
Compliance in mL/cmH_2O	27	32	34
Pulmonary artery catheter			
Baseline			
Mean PAP in mmHg	42	32	34
Systolic PAP in mmHg	57	42	44
PAOP in mmHg	7	9	11
CI in $L/min/m^2$	2.6	2.9	2.9
PVR in Wood Units	5.9	4.1	3.3
H1			
Mean PAP in mmHg	42	30	35
Systolic PAP in mmHg	65	39	41
PAOP in mmHg	8	9	13
CI in $L/min/m^2$	2.6	2.9	2.6
PVR in Wood Units	5.9	4.2	3.5
H2			
Mean PAP in mmHg	37	30	39
Systolic PAP in mmHg	52	33	45
PAOP in mmHg	8	11	14
CI in $L/min/m^2$	3.9	3.1	2.6
PVR in Wood Units	3.4	3.2	3.9
H12			
Mean PAP in mmHg	36	29	35
Systolic PAP in mmHg	50	49	40
PAOP in mmHg	6	11	10
CI in $L/min/m^2$	3.0	2.6	2.5
PVR in Wood Units	4.5	3.6	4.2
TEE-Right ventricular parameters			
Baseline			
RV FAC, %	45	42	58
RV outflow tract VTI in cm	19	13	19
H2			
RV FAC, %	44	42	34
RV outflow tract VTI in cm	16	15	24
H12			
RV FAC, %	48	34	42
RV outflow tract VTI in cm	15	16	19
TEE 2D-STE parameters			

Baseline			
RVGLS, %	13.5	25.3	14.8
TMAD septal in mm	13.0	29.7	23.5
H2			
RVGLS, %	13.3	24.7	22.7
TMAD septal in mm	9.6	27.6	25.0
H12			
RVGLS, %	16.9	25.0	18.7
TMAD septal in mm	16	32	23
ICU course			
Length of stay in d	30	32	31
Mechanical ventilation duration in d	18	22	21
Outcomes	Discharged from ICU	Discharged from ICU	Discharged from ICU

BMI: Body mass index; CI: Cardiac index; CT: Computed tomography; DAP: Diastolic arterial pressure; FAC: Fractional area change; GGO: Ground-glass opacity; H1: 1 h after almitrine infusion; H2: 2 h after almitrine infusion; H12: 12 h after almitrine infusion; HR: Heart rate; ICU: Intensive care unit; MAP: Mean arterial pressure; NO: Nitric oxide; PAP: Pulmonary artery pressure; PAOP: Pulmonary artery occlusion pressure; PBW: Predicted body weight; PEEP: Positive end-expiratory pressure; PVR: Pulmonary vascular resistance; RV: Right ventricle; RVGLS: Right ventricle global longitudinal strain; SAP: Systolic arterial pressure; SAPS II: Simplified acute physiology score; SOFA: Sepsis-related Organ Failure Assessment; STE: Speckle tracking echocardiography; TEE: Transesophageal echocardiography; TMAD: Tricuspid longitudinal annular displacement; VTI: Velocity time integral.

.

FINAL DIAGNOSIS

All three patients were admitted to the ICU for severe ARDS according to the Berlin definition with a PaO_2/FiO_2 ratio < 150. They were treated with protective ventilation (low tidal volume 6-7 mL/kg, PEEP for plateau pressure ≤ 30 cmH_2O), neuromuscular blocking agents and inhaled nitric oxide (at 10 ppm). Despite medical management they presented persistent severe hypoxemia.

TREATMENT

The local institutional review board waived the need for written informed consent; data storage was authorized by national licensing authority (CNIL PI2020_843_0026). Patients and/or next of kin were informed of the study. We prospectively collected data from three consecutive patients with COVID-19 and severe ARDS who received almitrine infusion.

Study evaluation

Low dose of almitrine (Vectarion®; Servier, Suresnes, France) was started at an infusion rate of 4 μg × kg × min^{-1}on a central line. The effect of almitrine infusion on respiratory parameters (blood gases, PaO_2/FiO_2 ratio, total respiratory system compliance) was evaluated. Pulmonary artery pressure (PAP), cardiac output and pulmonary vascular resistance (PVR) were monitored *via* a pulmonary artery catheter. RV FAC, RV global longitudinal strain and tricuspid longitudinal annular displacement were monitored *via* transesophageal echocardiography. Data were collected before and 1 h, 2 h and 12 h after almitrine infusion start.

Case 1: Almitrine infusion was started after 2 d of mechanical ventilation and sustained for 3 d.

Case 2: Almitrine was started at day 6 after ICU admission (5 d with high flow oxygen and 1 d under mechanical ventilation). Almitrine infusion was given for 3 d.

Case 3: Almitrine infusion was started after 2 d of mechanical ventilation. Almitrine infusion was given for 4 d.

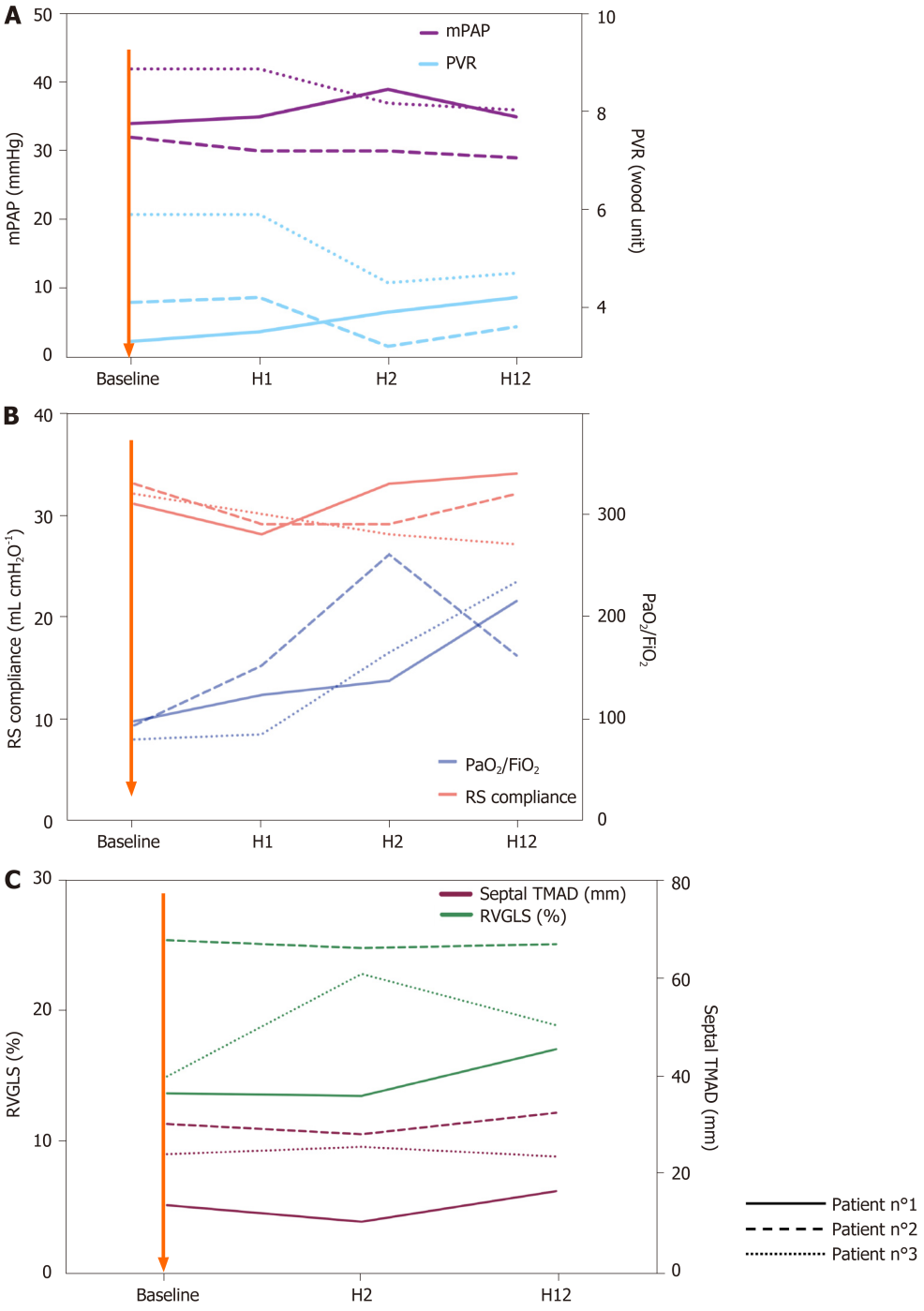

Figure 1 Evolution of pulmonary artery catheter, respiratory and echocardiographic parameters with almitrine infusion. A: Pulmonary artery pressure (PAP) and pulmonary vascular resistance (PVR) during almitrine infusion; B: PaO2/FiO2 ratio and total respiratory system compliance (CRS) during almitrine infusion; C: Right ventricular fractional area change (FAC) and right ventricular (RV) global longitudinal strain (RVGLS) remained unchanged for patient 1 and patient 2 and improved for patient 3. Tricuspid longitudinal annular displacement (TMAD) remained unchanged for the three patients.

OUTCOME AND FOLLOW-UP

ICU course

The PaO_2/FiO_2 ratio and total respiratory system compliance during almitrine infusion are presented in Figure 1 and Table 1. For the three patients, PaO_2/FiO_2 ratio time-course showed a dramatic increase whereas total respiratory system compliance was unchanged. The three patients were discharged from the ICU. ICU length of stay for patient 1, patient 2 and patient 3 was 30 d, 32 d and 31 d, respectively. Weaning from mechanical ventilation was performed 13 d, 18 d and 15 d after almitrine infusion for patient 1, 2 and 3, respectively.

Safety

Time-course of pulmonary artery catheter parameters and echocardiographic parameters during almitrine infusion are presented in Figure 1. PAP and PVR remained unchanged during almitrine infusion. Regarding RV function, RV FAC and RV global longitudinal strain remained unchanged for patient 1 and patient 2 and improved for patient 3. Tricuspid longitudinal annular displacement remained unchanged for the three patients. None of the patients needed extracorporeal membrane oxygenation therapy. Liver function test remained unchanged.

DISCUSSION

In this report, we found that almitrine infusion enhanced oxygenation of patients with severe COVID-19 related ARDS without any change in PAP and RV function. At baseline, the patients showed an increased PAP without pulmonary embolism and left ventricular dysfunction (normal pulmonary artery occlusion pressures and CI). Hence, we cannot discard the occurrence of at least a certain level of hypoxic pulmonary vasoconstriction that has been suggested by some authors[3].

In our patients, almitrine led to increased oxygenation without any changes in ventilatory parameters or right-side circulation. Hence, almitrine improved the ventilation/perfusion ratio by decreasing pulmonary flow. The lack of increase in PVR with almitrine is not in favor of an increase in hypoxic pulmonary vasoconstriction as encountered in typical ARDS. Recently, Ackermann *et al*[4] observed that the pulmonary histological pattern that distinguishes COVID-19 infected lungs from influenzae infected lung is the amount of new vessel growth in the COVID-19 lung. Moreover, Lang *et al*[1] studied lung perfusion by dual-energy chest CT scan for COVID-19 patients and found an increased perfusion of the lungs especially proximal to lung opacities. Increase of pulmonary vessels number is probably responsible of an intrapulmonary shunt with an increased ventilation/perfusion mismatch.

Almitrine acts as a selective pulmonary vessel vasoconstrictor that is able to decrease and redistribute pulmonary blood flow from shunt areas to pulmonary units with normal ventilation/pulmonary flow ratios[9]. We believe that the improvement in oxygenation with almitrine for our patients was related to a decrease in intrapulmonary shunt in both aerated and non-aerated lung regions[2]. Inhaled nitric oxide is a selective pulmonary vasodilator, and intravenously administered almitrine is a selective pulmonary vasoconstrictor. The resulting effects of combining almitrine and inhaled nitric oxide are likely related to the respective vascular effect of each drug on aerated and non-aerated lung compartments and explain why additive respiratory effects were observed. Previous studies confirmed that when reinforcing hypoxic pulmonary vasoconstriction by small doses of almitrine, the nitric oxide-induced increase in arterial oxygenation can be markedly enhanced[10,11].

The major risk with short term use of almitrine is the increase of RV afterload by excessive vasoconstriction. Hence, we evaluated RV function with very sensitive and reproducible parameters: RV global longitudinal strain and tricuspid longitudinal annular displacement[12,13]. We found no deleterious effects on RV function, which was similar to previous studies on almitrine safety[14]. Recently, Barthélémy *et al*[6] tested almitrine for COVID-19 patients, but crucial data on RV function was not reported.

CONCLUSION

Despite a small sample size, almitrine seems to be effective and safe to enhance oxygenation for COVID-19 critically ill patients. Further controlled studies are required.

REFERENCES

1 **Lang M**, Som A, Mendoza DP, Flores EJ, Reid N, Carey D, Li MD, Witkin A, Rodriguez-Lopez JM, Shepard JO, Little BP. Hypoxaemia related to COVID-19: vascular and perfusion abnormalities on dual-energy CT. *Lancet Infect Dis* 2020; **20**: 1365-1366 [PMID: 32359410 DOI: 10.1016/S1473-3099(20)30367-4]

2 **Mahjoub Y**, Rodenstein DO, Jounieaux V. Severe Covid-19 disease: rather AVDS than ARDS? *Crit*

Care 2020; **24**: 327 [PMID: 32527297 DOI: 10.1186/s13054-020-02972-w]

3 **Archer SL**, Sharp WW, Weir EK. Differentiating COVID-19 Pneumonia From Acute Respiratory Distress Syndrome and High Altitude Pulmonary Edema: Therapeutic Implications. *Circulation* 2020; **142**: 101-104 [PMID: 32369390 DOI: 10.1161/CIRCULATIONAHA.120.047915]

4 **Ackermann M**, Verleden SE, Kuehnel M, Haverich A, Welte T, Laenger F, Vanstapel A, Werlein C, Stark H, Tzankov A, Li WW, Li VW, Mentzer SJ, Jonigk D. Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19. *N Engl J Med* 2020; **383**: 120-128 [PMID: 32437596 DOI: 10.1056/NEJMoa2015432]

5 **Varga Z**, Flammer AJ, Steiger P, Haberecker M, Andermatt R, Zinkernagel AS, Mehra MR, Schuepbach RA, Ruschitzka F, Moch H. Endothelial cell infection and endotheliitis in COVID-19. *Lancet* 2020; **395**: 1417-1418 [PMID: 32325026 DOI: 10.1016/S0140-6736(20)30937-5]

6 **Barthélémy R**, Blot PL, Tiepolo A, Le Gall A, Mayeur C, Gaugain S, Morisson L, Gayat E, Mebazaa A, Chousterman BG. Efficacy of Almitrine in the Treatment of Hypoxemia in Sars-Cov-2 Acute Respiratory Distress Syndrome. *Chest* 2020; **158**: 2003-2006 [PMID: 32512007 DOI: 10.1016/j.chest.2020.05.573]

7 **Cardinale M**, Esnault P, Cotte J, Cungi PJ, Goutorbe P. Effect of almitrine bismesylate and inhaled nitric oxide on oxygenation in COVID-19 acute respiratory distress syndrome. *Anaesth Crit Care Pain Med* 2020; **39**: 471-472 [PMID: 32505755 DOI: 10.1016/j.accpm.2020.05.014]

8 **Losser MR**, Lapoix C, Delannoy M, Champigneulle B, Payen D. Almitrine as a non-ventilatory strategy to improve intrapulmonary shunt in COVID-19 patients. *Anaesth Crit Care Pain Med* 2020; **39**: 467-469 [PMID: 32505756 DOI: 10.1016/j.accpm.2020.05.013]

9 **Reyes A**, Roca J, Rodriguez-Roisin R, Torres A, Ussetti P, Wagner PD. Effect of almitrine on ventilation-perfusion distribution in adult respiratory distress syndrome. *Am Rev Respir Dis* 1988; **137**: 1062-1067 [PMID: 3195804 DOI: 10.1164/ajrccm/137.5.1062]

10 **Naeije R**, Lejeune P, Vachiéry JL, Leeman M, Mélot C, Hallemans R, Delcroix M, Brimioulle S. Restored hypoxic pulmonary vasoconstriction by peripheral chemoreceptor agonists in dogs. *Am Rev Respir Dis* 1990; **142**: 789-795 [PMID: 2121078 DOI: 10.1164/ajrccm/142.4.789]

11 **Gallart L**, Lu Q, Puybasset L, Umamaheswara Rao GS, Coriat P, Rouby JJ. Intravenous almitrine combined with inhaled nitric oxide for acute respiratory distress syndrome. The NO Almitrine Study Group. *Am J Respir Crit Care Med* 1998; **158**: 1770-1777 [PMID: 9847266 DOI: 10.1164/ajrccm.158.6.9804066]

12 **Li Y**, Li H, Zhu S, Xie Y, Wang B, He L, Zhang D, Zhang Y, Yuan H, Wu C, Sun W, Li M, Cui L, Cai Y, Wang J, Yang Y, Lv Q, Zhang L, Xie M. Prognostic Value of Right Ventricular Longitudinal Strain in Patients With COVID-19. *JACC Cardiovasc Imaging* 2020; **13**: 2287-2299 [PMID: 32654963 DOI: 10.1016/j.jcmg.2020.04.014]

13 **Beyls C**, Bohbot Y, Huette P, Abou-Arab O, Mahjoub Y. Tricuspid Longitudinal Annular Displacement for the Assessment of Right Ventricular Systolic Dysfunction during Prone Positioning in Patients with COVID-19. *J Am Soc Echocardiogr* 2020; **33**: 1055-1057 [PMID: 32561109 DOI: 10.1016/j.echo.2020.05.016]

14 **Esnault P**, Hraiech S, Bordes J, Forel JM, Adda M, Rambaud R, Lehingue S, Roch A, Papazian L, Guervilly C. Evaluation of Almitrine Infusion During Veno-Venous Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome in Adults. *Anesth Analg* 2019; **129**: e48-e51 [PMID: 29337729 DOI: 10.1213/ANE.0000000000002786]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com