OPIS PRZYPADKU / CASE REPORT
Otrzymano/Submitted: 11.03.2019 • Zaakceptowano/Accepted: 16.11.2019

Effective regional citrate anticoagulation during ECCO$_2$R in ARDS patient – case report

Joanna Zybura, Wojciech Mielnicki, Agnieszka Dyla
District Hospital in Olawa, Poland

Abstract

Background. Lung-protective ventilation is the most important concept in acute respiratory failure treatment (ARDS). Using this strategy might be seriously impeded by respiratory acidosis. Extracorporeal carbon dioxide removal during continuous renal replacement therapy (CRRT) might be helpful in treatment of such patients. ***Case report.*** We present a case of ARDS patient with CO_2 retention treated successfully with PrismaLung during CRRT with citrate anticoagulation. Therapy helped to decrease hypercarbia and improve respiratory acidosis that led to improvement of hemodynamic profile with reduction in catecholamine dosing. During this treatment the patient was ventilated according to ARDSNet protocol. ***Results.*** Such combined strategy resulted in quick patient improvement and successful overall treatment. Relatively short ventilation time and hospital stay resulted in absence of long-term complications as far as respiratory system is concerned. *Anestezjologia i Ratownictwo 2019; 13: 313-317.*

Keywords: ARDS, lung protective ventilation, extracorporeal CO_2 removal, citrate

Introduction

Lung-protective ventilation is the most important concept in acute respiratory failure (ARDS) [1]. Using this strategy might be seriously impeded by respiratory acidosis [2,3]. Extracorporeal carbon dioxide removal during continuous renal replacement therapy (CRRT) might be helpful in treatment of such patients [4-6]. We present a case of ARDS patient with CO_2 retention treated successfully with PrismaLung during CRRT with citrate anticoagulation.

Case report

Forty-thee year old patient without relevant past medical history was admitted to Intensive Care Unit (ICU) from Emergency Department with septic shock due to severe pneumonia. On admission to ICU the patient was in serious condition (SAPS 43, SOFA 8), he remained conscious, restless and complaining of severe dyspnea. On physical exam he was tachypneic with respiratory effort and bilateral crackles with oxygen saturation (SpO_2) 79-83% on high flow oxygen via facemask. Norepinephrine infusion was initiated at the dose of 0.18 mcg/kg/min, mean arterial pressure (MAP) of 60-65 mmHg was reached and HR of 140/min. In the chest X-ray there were bilateral parenchymal opacities. Lung ultrasound showed bilateral B-lines. There was also lung consolidation on the left side. Alveolar-interstitial syndrome was recognized. After exclusion of LV dysfunction with echocardiography, ARDS was diagnosed (PaO_2/FiO_2 - 102). Microbiological material was taken and empiric antibiotic therapy was started (levofloxacin, ceftriaxone) for community acquired pneumonia. The patient was intubated and started on mechanical ventilation with ARDSNet protocol.

In the following hours the patient hemodynamically deteriorated. Epinephrine infusion was started -0.05 mcg/kg/min and subsequently vasopressin – 0.01-0.02 µ/min. Hemodynamic monitoring was mainly ultrasound-guided. The patient was also continuously monitored by LidcoRapid. During the first 24 hours of therapy the patient was evaluated as hypovolemic. In the repeated TTE LV (transthoracic

echocardiography) function was preserved with EF 65%, LVOT (left ventricular outflow tract) 1.54 m/s, VTI (velocity time integral) 18-20 cm. Passive leg raising (PLR) test stayed positive in spite of fluid therapy. These findings were confirmed in LidcoRapid (CI – cardiac index – 1.2-2.2 l/min/m^2, SVV 15-20%, SVR 1200-2000 dynes sec/cm^5/m^2). Fluid therapy and vasopressors were continued. Due to prolonged fluid necessity, the patient achieved +7000 ml fluid balance in 48 hours therapy.

In spite of protective ventilation (SIMV-VC with VT (tidal volume) 5 ml/kg, PEEP levels 12-16 cm, Pplat < 30 cm H_2O), recruitment maneuvers, deep sedation and muscle paralysis the oxygenation did not improve (PaO_2/FiO_2 – 100, driving pressure – 10-14 cm H_2O). After 10 hours of ICU treatment 18 hour sessions of prone position were initiated. Oxygenation improved but CO_2 retention started with hypotonia. Based on laboratory tests (creatinine 2.9 mg/dl) and low urine output (< 0.3 ml/kg/h for 24 h) acute kidney injury was diagnosed. After 30 hours of treatment CRRT was started in CVVHDF mode (PrismaFlex Baxter) with citrate anticoagulation and PrismaLung for CO_2 removal. The flows during CVVHDF and control of anticoagulation are presented in Table I. Sweep gas flows of 10 l/min were used during $ECCO_2R$. In the following hours citrate flow was reduced with Ca++ post filter and Ca total/Ca++ ratio regularly monitored to diagnose potential citrate accumulation and intoxication.

After therapy initiation CO_2 level dropped substantially with respiratory acidosis improvement (Table II) leading to dose reduction of catecholamines (Figure 1). After 1 2 h of $ECCO_2R$ hemodynamic profile has changed. LVEF (left ventricle ejection fraction) deteriorated to 40%, MV (mitral valve) inflow pattern was restrictive (E/A > 2), PLR test was negative. In LidcoRapid we found CI 2.0 l/min/m^2, SVV 4%, SVR 3000 dynes sec/cm^5/m^2. Fluid removal was initiated during CRRT, blood flow reduced to 150 ml/h and $ECCO_2R$ was continued for 72 h.

Table II. Improvement of gas exchange parameters and acid-base balance during therapy

hours after start	PaO_2	$PaCO_2$	pH	FiO_2	PaO_2/FiO_2
0	81,8	91	7,04	0,75	109
+1	80,1	82,4	7,07	0,75	106
+2	101	70,2	7,12	0,75	134
+3	127	67,4	7,16	0,75	169
+4	158	66,1	7,19	0,75	210
+5	120	61,7	7,22	0,65	184
+6	135	61,7	7,23	0,65	207
+7	132	58,9	7,25	0,65	203
+8	135	58	7,27	0,65	207
+12	135	57,4	7,28	0,60	225
+18	150	57,4	7,28	0,60	250
+24	150	59,4	7,29	0,55	272

Table I. The flows and control of anticoagulation during CVVHDF with $ECCO_2R$

	blood flow [ml/min]	citrate flow [ml/h]	dializate flow [ml/h]	substytute flow [ml/h]	CaCl2 comp [%]	effluent dose [ml/kg/h]	post-filter Ca^{2+} [mmol/L]	Ca/Ca^{2+} ratio
0	300	3000	700	200	100	41		
+1	300	3000	700	200	100	41	0,45	
+2	300	3000	700	200	120	39	0,3	1,90
+3	300	2600	900	200	130	39	0,32	
+4	300	2400	900	200	130	37	0,35	
+5	300	2400	900	200	130	37	0,43	
+6	300	2500	900	200	130	37	0,4	1,95
+7	300	2500	900	200	130	37	0,41	
+8	300	2500	900	200	130	37		
+12	150	1250	900	200	130	37	0,42	
+18	150	1250	900	200	130	37	0,56	1,96
+24	150	1800	900	200	130	37		
+36	100	900	800	200	100	21	0,42	1,9
+48	100	900	800	200	80	21	0,43	1,89
+60	100	967	800	200	75	22	0,41	2,01
+72	100	1000	800	200	90	22	0,41	2,11

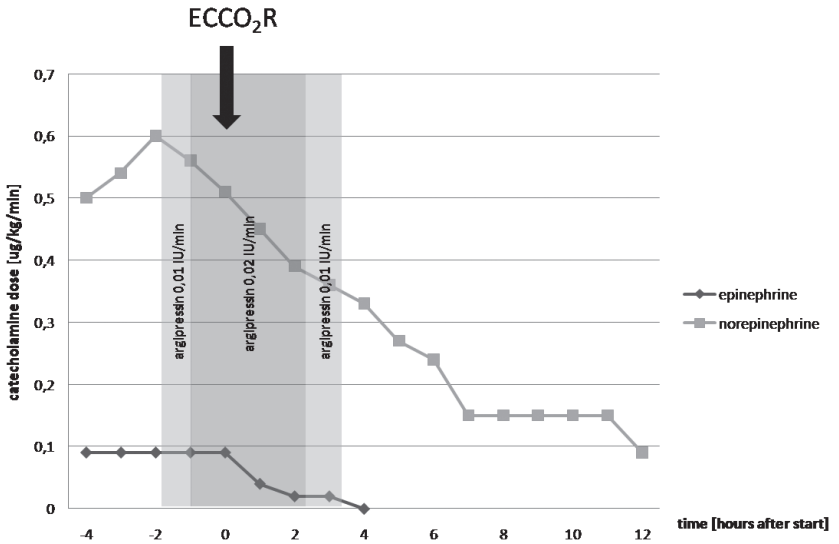

Figure 1. Catecholamin and argipressin dose reduction after CO_2 removal with $ECCO_2R$

In the third day of ICU treatment the patient was stable, Streptococcus pneumoniae was confirmed and targeted therapy was continued. On the 4th day of ICU treatment catecholamines were stopped, on 10th day he was extubated, on 14th day CRRT was stopped. The patient was discharged from ICU on 20th day and from hospital on 25th day.

Discussion

Severe ARDS in ICU patients can be a life-threatening condition with high mortality [7,8]. According to updated definition, ARDS diagnosis is based on clinical, radiological and oxygenation criteria [9]. Bilateral opacities should be detected in lung CT scan. However, lung ultrasound was shown to be useful and reliable method in ARDS diagnosis and management [10-12]. In our team we have been using lung ultrasound successfully for years in many clinical situations. In ARDS patients this method is especially useful as noninvasive and easily performed at the bedside. It is also possible to use it during prone position. Based on literature and our experience we have completely stopped performing chest CTs in ARDS management.

Protective ventilation with low VT (tidal volume), low Pplat and low driving pressure lead to improvement of outcome [1]. In patient with PaO_2/FiO_2 ratio ≤ 150 prone positioning with muscle paralysis is strongly recommended to decrease mortality [13]. Further lowering the driving pressure and VT might be additionally beneficial in ARDS treatment [1]. Using such ventilation targets may lead to CO_2 retention and respiratory acidosis. High CO_2 levels may lead to increased ICP, pulmonary hypertension, decreased inotropy of the heart, decreased kidney perfusion and release of endogenic catecholamines. Extracorporeal CO_2 removal ($ECCO_2R$) might facilitate ultraprotective ventilation, limit ventilator induced lung injury [4] and limit the consequences of hypercarbia.

Despite the wide use of regional citrate anticoagulation in many extracorporeal systems in intensive care [14,15] heparin remains the most commonly used anticoagulant in CO_2 removal systems. The main reason is that we use higher blood flow rates in these systems. Simultaneously, citrate load would be actually high. This problem might be serious in patients predisposed for citrate accumulation, due to reduced metabolism: in liver failure, MOF and severe metabolic acidosis [16]. That may be the reason why the usage of regional anticoagulation in $ECCO_2R$ hasn't been prevalent. We can find some animal models [17,18] suggesting that regional anticoagulation with citrate could be alternative option.

Because of our good experience with citrates anticoagulation in many clinical situations, including severe liver failure [19] we decided to use it in presented case. During $ECCO_2R$ Ca total/Ca++ ratio was strictly monitored and remained on safe level (Ca total/Ca++

< 2.5). To minimize the risk of citrate accumulation, blood flows were reduced after 12 hours of therapy without loss of CO_2 removal effectiveness.

In the presented case, PrismaLung therapy during CVVHDF with citrate anticoagulation helped to decrease hypercarbia and respiratory acidosis that might have improved hemodynamic profile with reduction in catecholamine dosing. During this treatment the patient was ventilated according to ARDSNet protocol. Such combined strategy resulted in quick patient improvement and successful overall treatment.

Conclusions

In the presented case, usage of extracorporeal CO_2 elimination with PrismaLung during CRRT with regional citrate anticoagulation enabled continuous protective ventilation in spite of high initial CO_2 levels. Reduction of hypercarbia and respiratory acidosis led to quick patient stabilization and improvement in acid--base balance. Regional citrate anticoagulation proved to be effective and safe mode of anticoagulation in spite of high risk of accumulation of citrate. Relatively short ventilation time and hospital stay resulted in absence of long-term complications as far as respiratory system is concerned.

Conflict of interest
None

Correspondence address
Agnieszka Dyla
Oddział Anestezjologii i Intensywnej Terapii
Zespół Opieki Zdrowotnej w Oławie
ul. K. K. Baczyńskiego 1; 55-200 Oława
☎ (+48 71) 301 13 97
dylusia@wp.pl

References

1. Acute Respiratory Distress Syndrome Network, Brower RG, Matthay MA, Morris A, Schoenfeld D, Thompson BT, et al. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med. 2000;342(18):1301-8.
2. Carvalho CR, Barbas CS, Medeiros DM, Magaldi RB, Lorenzi Filho G, Kairalla RA, et al. Temporal hemodynamic effects of permissive hypercapnia associated with ideal PEEP in ARDS. Am J Respir Crit Care Med. 1997 Nov;156(5):1458-66.
3. Kiiski R, Takala J, Kari A, Milic-Emili J. Effect of tidal volume on gas exchange and oxygen transport in the adult respiratory distress syndrome. Am Rev Respir Dis. 1992 Nov;146(5 Pt 1):1131-5.
4. Schmidt M, Jaber S, Zogheib E, Godet T, Capellier G, Combes A. Feasibility and safety of low-flow extracorporeal CO2 removal managed with a renal replacement platform to enhance lung-protective ventilation of patients with mild-to-moderate ARDS. Crit Care Lond Engl. 2018;22(1):122.
5. Grant AA, Hart VJ, Lineen EB, Forsberg BC, Klima A, Mirsaeidi M, et al. Rescue therapy for hypercapnia due to high PEEP mechanical ventilation in patients with ARDS and renal failure. Artif Organs. 2019 Jun;43(6):599-604.
6. Peperstraete H, Eloot S, Depuydt P, De Somer F, Roosens C, Hoste E. Low flow extracorporeal CO2 removal in ARDS patients: a prospective short-term crossover pilot study. BMC Anesthesiol. 2017 Nov 28;17(1):155.
7. Dushianthan A, Grocott MPW, Postle AD, Cusack R. Acute respiratory distress syndrome and acute lung injury. Postgrad Med J. 2011 Sep;87(1031):612–22.
8. Phua J, Badia JR, Adhikari NKJ, Friedrich JO, Fowler RA, Singh JM, et al. Has mortality from acute respiratory distress syndrome decreased over time?: A systematic review. Am J Respir Crit Care Med. 2009 Feb;179(3):220-7.
9. Ferguson ND, Fan E, Camporota L, Antonelli M, Anzueto A, Beale R, et al. The Berlin definition of ARDS: an expanded rationale, justification, and supplementary material. Intensive Care Med. 2012 Oct;38(10):1573-82.
10. Chaari A, Bousselmi K, Assar W, Kumar V, Khalil E, Kauts V, et al. Usefulness of ultrasound in the management of acute respiratory distress syndrome. Int J Crit Illn Inj Sci. 2019;9(1):11-5.
11. Rode B, Vučić M, Siranović M, Horvat A, Krolo H, Kelečić M, et al. Positive end-expiratory pressure lung recruitment: comparison between lower inflection point and ultrasound assessment. Wien Klin Wochenschr. 2012 Dec;124(23-24):842-7.
12. Stefanidis K, Dimopoulos S, Tripodaki E-S, Vitzilaios K, Politis P, Piperopoulos P, et al. Lung sonography and recruitment in patients with early acute respiratory distress syndrome: a pilot study. Crit Care Lond Engl. 2011 Aug 4;15(4):R185.
13. Kamo T, Aoki Y, Fukuda T, Kurahashi K, Yasuda H, Sanui M, et al. Optimal duration of prone positioning in patients with acute respiratory distress syndrome: a protocol for a systematic review and meta-regression analysis. BMJ Open. 2018;8(9):e021408.

14. Bagshaw SM, Laupland KB, Boiteau PJE, Godinez-Luna T. Is regional citrate superior to systemic heparin anticoagulation for continuous renal replacement therapy? A prospective observational study in an adult regional critical care system. J Crit Care. 2005 Jun;20(2):155-61.
15. Wu M-Y, Hsu Y-H, Bai C-H, Lin Y-F, Wu C-H, Tam K-W. Regional citrate versus heparin anticoagulation for continuous renal replacement therapy: a meta-analysis of randomized controlled trials. Am J Kidney Dis Off J Natl Kidney Found. 2012 Jun;59(6):810-8.
16. Citrate anticoagulation for continuous renal replacement therapy in critically ill patients: success and limits. - PubMed - NCBI [Internet]. [cited 2019 Oct 2]. Available from: https://www.ncbi.nlm.nih.gov/pubmed/?term=mariano+bergano+gangemi
17. Cardenas VJ, Miller L, Lynch JE, Anderson MJ, Zwischenberger JB. Percutaneous venovenous CO2 removal with regional anticoagulation in an ovine model. ASAIO J Am Soc Artif Intern Organs 1992. 2006 Aug;52(4):467-70.
18. Sharma AS, Weerwind PW, Bekers O, Wouters EM, Maessen JG. Carbon dioxide dialysis in a swine model utilizing systemic and regional anticoagulation. Intensive Care Med Exp. 2016 Dec;4(1):2.
19. Dyla A, Mielnicki W, Bartczak J, Zawada T, Garba P. Effectiveness and Safety Assessment of Citrate Anticoagulation During Albumin Dialysis in Comparison to Other Methods of Anticoagulation. Artif Organs. 2017 Sep;41(9):818-26.