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A TREATMENT MODALITY PROMISING SURVIVAL IN ARDS DESPITE COMPLICATION: ECMO

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ABSTRACT
The primary treatment principle of acute respiratory distress syndrome (ARDS) proceeding with high morbidity and mortality in intensive care unit is the protective mechanical ventilation strategies. While extracorporeal ventilation has not become a standard treatment, it has taken part as a new treatment modality in cases in which classical ventilation methods are insufficient. Hereby we aimed to present an ARDS case treated with extracorporeal membrane oxygenation (ECMO) who developed disseminated intravascular coagulation (DIC) during the course.

INTRODUCTION

Acute respiratory distress syndrome (ARDS) is a hypoxemic respiratory failure characterized by non-cardiac pulmonary edema caused by permeability increase in alveolo-capillary membrane. Other significant clinical characteristics of ARDS are bilateral diffuse infiltrations and resistant hypoxemia to oxygen treatment [1]. Mechanical ventilation (MV) strategies lie in the first place in basic treatment plan in ARDS. Reduction of iatrogenic damage depending on mechanical ventilation in ARDS is the only precise proven initiative which decreases mortality. Ventilation with lower tidal volumes are compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome [2]. High PEEP and lower tidal volumes are applications diminishing iatrogenic damage called as lung protective ventilation, and they form the main principle of ARDS treatment today. Because lower tidal volume inhibits barotrauma and high PEEP application, however, prevents cyclic atelectasis, they allow atelectrauma to be precluded. Although extracorporeal ventilation (EV), high frequency ventilation and liquid ventilation are not involved in standard treatment, they have indicated promising consequences over clinical results. Of the alternative treatment methods, particularly EV and extracorporeal membrane oxygenation (ECMO) have come to be used in ARDS cases that are unresponsive to current treatments today. It is shown with clinical studies that ECMO improves the survival rate. Nevertheless, adverse effects can be observed during treatment period [3].

In this case report, in a patient who had undergone appendectomy in the presence of available respiratory tract infection and developed ARDS in the postoperative period, we aimed to point out the importance of ECMO that could be a lifesaving treatment option and complications which could develop throughout this process.

CASE REPORT

A 13 year-old female patient was transferred to our intensive care unit from another center to undergo ECMO due to ARDS development in the postoperative period following laparoscopic appendectomy and being unresponsive to conventional MV strategies and prone positioning. It was learnt that the patient undergoing respiratory tract infection prior to operation had developed respiratory distress syndrome in the postoperative period. Despite a 15-day mechanical ventilation support, the patient whose weaning trials failed was operated for bedside percutaneous tracheotomy. In the follow-ups, the patient was diagnosed as ARDS under sychronized intermittant ventilation (SIMV) mode, inspired fractional oxygen (FiO_2) rate: 60%, Positive End-Expiratory Pressure (PEEP): 12 cmH_2O, pressure over PEEP (PEEP'): 26 cmH_2O, tidal volume (TV): 320 ml (6.4 ml/ibw) and respiratory rate (RR): 35/min with the arterial blood gases (ABG) as pH: 7.41, partial arterial oxygen pressure (PO_2): 46.8 mmHg, partial arterial carbondioxide pressure (PCO_2): 47 mmHg and oxygen saturation (SpO_2): 89%. In the physical examination, diffuse rhonchi was detected in the lung auscultation, and respiratory sounds decreased at the base. Sedation was instituted with 2 mcg/kg/min remifentanyl infusion. Treatment intended for reducing tidal volumes and protective mechanical ventilation strategy was established. All culture samples were collected, and a broad spectrum antibiotherapy was commenced [colistin 2x150 mg intravenous (IV) and 2x75 mg nebulized, 3x1 gr sulbactam sodium/ cefoperazone sodium IV and 1x400 mg teicoplanin IV]. Inhaler bronchodilator and anti-inflammatory agents were added to treatment (budesonide, ipratropium bromide, N-acetylcysteine, magnesium and adrenalin nebules). Ground glass appearances and patchy infiltrations were observed in both lungs in thorax computed tomography (CT) (Figure.1). Pressures were re-increased owing to impairment in blood gas of the patient on 5th day proceeded by decreasing fluid balance intermittently under hemodiafiltration in the course of 4 days. It was determined that while the values were as follows; FiO_2: 60 %, PEEP/PEEP': 13/20 , RR: 27/min,TV: 280 ml (5.6 ml/ibw), ABG values were identified as pH: 7.47, PO_2: 50 mmHg, PCO_2: 57.2 mmHg, SPO_2: 83 %. ECMO application was decided for the patient whose Horowitz ratio was hardly raised from 78 to only 83.3 with all these effort and measures. Membrane ventilator (Novalung ILA-active) was attached to patient by placing 21 french (F) catheter into right femoral vein and 18 F into right internal jugular vein under general anesthesia with the centrifugal rate of 2500 rpm to provide a blood flow of 3000 ml/min with sweep gas flow of 7 lt/min and fiO_2: 80 %. The patient was infused with heparin to achieve an activated clotting time (ACT) in the range of 150-200 seconds. Hemodiafiltration was continued over ECMO. Sufficient oxygenation was achieved at lower tidal volumes with the aid of ILA membrane ventilator. Mechanical ventilation values of the patient on the 10th postECMO day were FiO_2 35%, PEEP/PEEP': 5/12, TV:200 ml, on the other hand, blood gas values were pH:7.38, PO_2: 115 mmHg, PCO_2:45.4 mmHg (Table 1). ECMO treatment was stopped on its 11th day as the catheter in the right vein was dislocated during patient care.

Table 1. Mechanical ventilation parameters and blood gases profile of the patient before and after extracorporeal ventilaton together with the changes on ECMO machine

Parameters	PreECMO	ECMO day 0	ECMO day 1	ECMO day 5	ECMO day10	PostECMO day15
PEEP (cmH_2O)	12	13	10	8	5	5
PEEP'(cmH_2O)	26	20	18	14	12	10
TV (ml)	320	280	200	180	200	345
pH	7,41	7,40	7,56	7.34	7.38	7.40
pCO_2 (mmHg)	47	57.2	38	41	45.4	38
pO_2 (mmHg)	46.8	50	92	104	115	102
FiO_2	0.6	0.6	0.5	0.35	0.35	0.3
Horowitz index	78	83.3	184	297	328	340
Blood flow (ml/min)	-	-	3000	2200	1500	-
Sweep gas flow (l/min)	-	-	7	5	3	-
ECMO FiO_2	-	-	0,8	0.5	0.4	-

ECMO: extracorporeal membrane oxygenation, PEEP: positive end-expiratory pressure, PEEP': pressure over PEEP, TV: tidal volume, FiO_2: fractional inspired oxygen

During ECMO, the thrombocyte count was within normal ranges in daily measurements (N: 150.000-400.000), but a decrease to 57000/mm^3 was noticed on the second day after termination of ECMO. Together with this decrease in thrombocytes, lactate level was 117 mg/dl, fibrinogen was 86 mg/dl (N: 238-493), D-dimer was 21.600 µIU/L (N: 80-500), prothrombin time (PT) was 38.4 sec (N: 9.4-12.5), active partial thromboplastin time (aPTT) was 44.2 sec (N: 25.1-36.5) for the patient. Therewith the patient was diagnosed with disseminated intravascular coagulation (DIC). The symptomatic supportive care was provided for the patient who had no major bleeding except bleeding from tracheostomy

cannula, and her condition of DIC started to regress beginning from the third day without any extra treatment other than single cure fibrinogen replacement. It was determined on the 5th day of DIC that the number of thrombocytes was 143.000/mm³ and lactate level 28.2 mg/dl, fibrinogen 158 mg/dl, D-dimer 12.500 µIU/L, PT 17.2 sec and aPTT 28.7 sec. During this period, the patient whose respiratory mechanics recovered was followed five more days with mechanical ventilator support in pressure support mode and T-tube intermittently, then was weaned from mechanical ventilation. It was identified in thorax CT taken after seven days following ECMO that there was a significant decline in the consolidation areas compared to the first CT (Figure.2). After a few days with supportive measures in the ICU, the patient was discharged home after her tracheotomy had been closed.

Figure 1. Bilateral infiltrates and ground glass appearance in thoracal CT consistent with acute respiratory distress syndrome (ARDS)

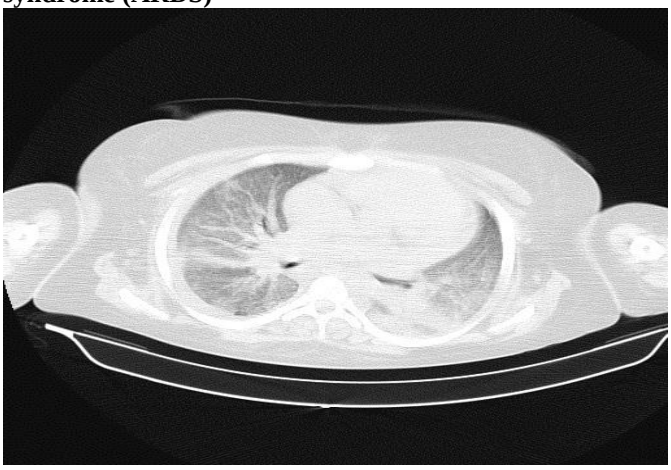
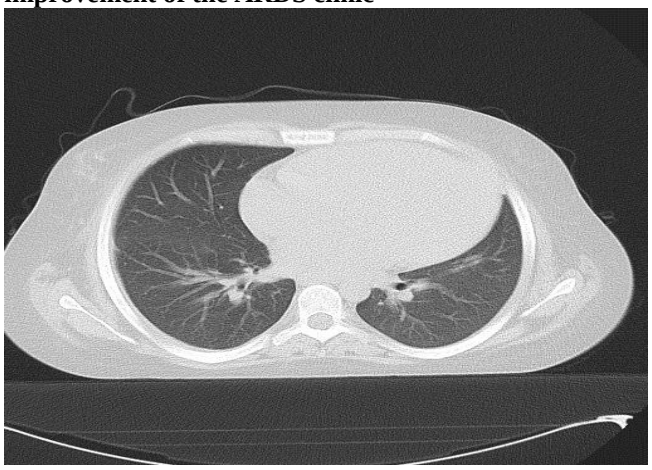


Figure 2. Thoracal CT images after completion of extracorporeal ventilation therapy showing the improvement of the ARDS clinic



DISCUSSION

ARDS was first defined by Ashbaugh and Petty as an adult respiratory distress syndrome in 1967 [1]. In this report, they defined rapidly developing acute respiratory failure characterized by tachypnea, dyspnea, refractory hypoxemia, diffuse bilateral infiltrates and reduction in lung compliance in 12 patients. ARDS is described as acute and persistent lung inflammation accompanied by severe hypoxia clinically in conjunction with vascular permeability increase. It is diagnosed by clinical findings and imaging methods. Pulmonary edema characterized by diffuse alveolar damage, severe hypoxemia resistant to oxygen treatment, decreased pulmonary compliance and a clinical picture proceeding with bilateral alveolar infiltration in the lung radiography are the characteristics [4].The criteria in the description of ARDS in 2012 have been revised [5]. According to this description our patient is compatible with moderate ARDS; however, she was applied ECMO as weaning conditions could not be achieved despite protective mechanical ventilation application for 15 days in another center and in our clinic for 5 days.

While the mortality rates of patients with ARDS were reported as 50%, its prognosis mostly depends on lung damage or if available, the severity of accompanying extrapulmonary disease. It was indicated in the analyses that ARDS mortality is associated with age (>70), presence of liver cirrhosis, APACHE II (the acute physiology and chronic health evaluation II) score and SOFA (sequential organ failure assessment) score.[6] APACHE score of our patient at the time of hospitalization was 13, and SOFA score was 5. As to mortality rate, two independent risk factors were described related to the lungs. They are the direct lung damage in ARDS etiology and the degree of oxygenation on the third day following ARDS introduction [7].

Permissive hypercapnia and protective lung ventilation strategies have taken their places as standard [2]. ECMO, high frequency ventilation, prone position and other pharmacological treatments can only be applied by experienced individuals in severe ARDS conditions in which no response can be obtained with standard treatment [5]. Of the treatment methods, ECMO helps lung to get better by inhibiting baro- and volutrauma in ARDS cases that are unresponsive to all mechanical ventilation strategies [3,8]. ECMO, also referred to as "ultraprotective ventilation", is a new and above all lifesaving treatment methods allowing lung to recover, decreasing the time the patient spends on mechanical ventilator. ECMO provides O_2 diffusion to blood circulation that is taken outside of the body as venovenous or arteriovenous, and it also supplies CO_2 elimination. In this technology, membrane oxygenators and thin membranes allowing oxygenation are used. Extracorporeal carbondioxide removal is one of the basic treatment mechanisms. The most important randomized controlled study comparing ECMO and conventional treatment was published by Peek GI et al. in Lancet in 2009. In this study, it was found out that while 6-

month survival period was 47% in the conventional group, it was 63% in ECMO group. In addition, cost-effectiveness was evaluated, and analyses were determined in favour of ECMO in the study [8].

ECMO is an extracorporeal treatment method and is applied to patients with heparin infusion. Complication rate is frequent due to both heparin infusion and catheter application. In the meta-analysis by Zangrillo et al. published in 2013, ECMO complications and mortality rates were examined [3]. In 12 studies involved in the analysis, the data regarding 1763 patients were studied. It was determined that the number of ECMO-applied median days were 5.9, mortality throughout ECMO was 45%, mortality rate for 30 days was 54%, and mortality following ECMO was 13%. Venoarterial was carried out in 92% of patients and mortality risk was found lower in venovenous ECMO compared to venoarterial. It was established that pediatric age group, sex and ECMO duration were not associated with mortality in reference to analysis results. Most frequently seen complications were respectively determined as renal failure requiring CVVHF (52%), bacterial pneumonia (33%), bleeding (33%), impairments as to oxygenator requiring system to be modified (29%), sepsis (26%), hemolysis (18%), liver dysfunctions (16%), leg ischemia (10%), venous thrombosis (10%), central nervous system complications (8%), GIS bleeding (7%), aspiration pneumonia (5%), DIC (5%). In another study released in 2012, 14 patients who achieved ECMO treatment during influenza outbreak in Japan in 2009 were examined [9]. ECMO treatment duration was reported as 8.5 days. Complications developed in all patients except for one who died on the first day of ECMO treatment and complications related to ECMO device were seen as 78.6 %. Of all, most frequently encountered one was problems as to oxygenator with 50%. Among the complications developed in patients during ECMO treatment, the most frequent one was DIC with 71.4%, and it was followed by massive bleeding with 57.1% (among these, surgical area bleeding (28.6%), upper GI bleeding (28.6%), bleeding in cannulation (14.3%) and pulmonary hemorrhage accounted for 7.1%). Other developed complications were defined as hemolysis (14.3%) and venous thrombosis (14.3%). As seen above, different results were reported particularly in terms of DIC development amid the frequency of complications in studies conducted. Long term treatment was thought to be the cause of DIC development in our current case that was applied ECMO treatment for a total of 11 days.

Further studies are required for these treatments to be involved in standard treatment strategies since they were shown to be useful in only small series. We performed a successful treatment in the light of all this information with ILA membrane ventilator in our ARDS case that had been supported by mechanical ventilation for a long time but unresponsive to it. She is still living a healthy life on the 23rd month after she had been discharged from our intensive care unit. ECMO in ARDS appears to be a treatment that can increase survival despite potential complications if managed well.

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