

## Recompensation of a therapy-resistant respiratory acidosis in severe sepsis with a pumpless extracorporeal CO<sub>2</sub>-elimination system

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### Abstract

Sepsis is not uncommon in intensive care, often leading to multiorgan dysfunction (MODS) or multiorgan failure (MOF). In case of a pulmonary dysfunction/failure oxygenation and/or carbon dioxide removal are impaired. This leads to hypoxia, respiratory acidosis and cardiocirculatory depression. The acidosis is aggravated by permissive hypercapnia when applying lung protective ventilation. The new pumpless extracorporeal lung assist system (pECLA) provides extracorporeal CO<sub>2</sub>-elimination and thus reduces the side effects of lung protective ventilation.

We report about the recompensation of a therapy-resistant respiratory acidosis in a septic patient with severe pneumonia by the use of a pECLA system.

### Introduction

Despite advanced therapeutic strategies and new antibiotic substances sepsis and septic complications like multiorgan dysfunction syndrome (MODS) or multiorgan failure (MOF) are still a major cause for death on intensive care units. Advanced sepsis treatment involves not only surgical debridement, but also “early goal-directed therapy” with volume resuscitation, maintaining an adequate hematocrit and cardiac output (3). Additionally, restricted adjustment of blood glucose should be applied (4). Pharmacological means include, among others, the use of activated protein C, an

initial broad-spectrum antibiotics and the application of low-dose hydrocortisone (2).

The majority of septic patients requires an artificial ventilation since the lung is a frequently affected organ, either primarily or secondarily. To reduce the ventilator-induced lung injury (VILI), lung protective ventilation with small tidal volumes and permissive hypercapnia is state-of-the-art (2). Unfortunately, hypercapnia and the resulting respiratory acidosis impair myocardial contractility and are limited by hemodynamic instability (6, 7).

The pumpless arteriovenous system for extracorporeal CO<sub>2</sub> elimination (pumpless extracorporeal lung

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assist, pECLA; NovaLung GmbH, Hechingen, Germany), which has recently become available, offers the possibility of efficient treatment. The transport of the blood through the pECLA is passive via the pressure gradient between the femoral artery and vein. CO<sub>2</sub> is eliminated from the blood by diffusion, thus diminishing the acidosis (for a detailed description see Bein et al. [8, 11]).

Thus far, the indication for using a pECLA is conventionally uncontrollable acidosis (pH < 7.2) due to hypercapnia in acute pulmonary damage, such as acute lung injury (ALI) or ARDS or pneumonia/sepsis. Initial results indicate a marked improvement in the survival rate of these patients [8, 9, 10, 11], although a prognostic evaluation of the procedure is not possible due to the small number of cases thus far.

We are reporting here about a patient with therapy-resistant respiratory acidosis due to severe pneumonia and sepsis who was successfully treated with a guideline-oriented complex sepsis therapy and the use of a pECLA device.

## Case report

The 44-year-old man was admitted to hospital due to an odontogenic throat abscess. Broad abscess areas were revealed by neck and thorax CT in the oropharynx and throat, which extended from dorsal to the trachea and esophagus, around the subclavic artery to the level of the tracheal bifurcation. Moreover, alveolar pulmonary infiltrates were found in the lower right lobe, indicating bronchopneumonia. The patient underwent surgical debridement of neck and oropharynx and was transferred to the intensive care unit sedated and intubated.

Due to the clinical presentation of severe sepsis (SAPS II 40 points, CRP 132.0 mg/L; PCT 16.71 ng/mL) with hypotensive cardiovascular status (RR 100/60 mmHg, HR 130/min, CVP 4 mmHg; ScvO<sub>2</sub> 67%), sepsis therapy with activated Protein C (Xigris®, Lilly), calculated broad-spectrum antibiotics and hydrocortisone (0.18 mg/kg/h) according to current guidelines and an “early goal-directed therapy” with restrictive adjustment of blood glucose (80-110 mg/dL), adequate hematocrit (>30) and adequate volume therapy (target CVP 12 mmHg) was initiated. Initially, inotropics (dobutamine 2 µg/kg/min) and vasopressors (norepinephrine 0.2 µg/kg/min) were required. By all these means, hemodynamic stabilization was achieved; administration of norepinephrine could

be withdrawn on the first day of treatment. Cardiac monitoring consisted of arterial blood pressure (ABP) and central venous pressure (CVP); a PICCO® system was used after initial stabilisation.

The patient presented on the first day of treatment with CO<sub>2</sub> retention with a 24-h mean value of the CO<sub>2</sub> partial pressure of 57.3 mmHg (7.64 kPa), which was progredient during the following three days of treatment and required increasingly aggressive ventilation [AF 20/min; p<sub>max</sub> 32 mbar; PEEP 14 mbar; V<sub>t</sub> 0.73 L; AMV 14.6 L/min]. The thorax X-ray revealed a newly-occurring pneumonic infiltrate in the lower left field, but did not provide an explanation for the pronounced hypercapnia. Due to the serious pneumonia and hypercapnia, surgical debridement of the mediastinal abscess could not be performed with justifiable risk. The respiratory acidosis could also not be brought under control with aggressive ventilation [AF 18/min; p<sub>max</sub> 36 mbar; PEEP 15 mbar; V<sub>t</sub> 1.18 L; AMV 21.2 L/min] and the use of buffer substances [pH 7.033; HCO<sub>3</sub><sup>-</sup> 30 mmol/L; paCO<sub>2</sub> 112.1 mmHg (14.95 kPa); paO<sub>2</sub> 162 mmHg (21.6 kPa); FiO<sub>2</sub> 0.9]. This was accompanied by a considerable increase in catecholamine requirement (norepinephrine up to 0.9 µg/kg/min). As ultima-ratio therapy in progredient hypercapnia, the decision was taken to use the pECLA system.

After connecting the pECLA on the sixth day of treatment, ventilation could be greatly deescalated (Figure 1). Within one hour, the peak pressure could be reduced from 38 mbar to 28 mbar, the tidal volume from 1180 to 510 mL; the paCO<sub>2</sub> decreased in the 24-h mean from 75.75 mmHg (10.1 kPa) to 45.5 mmHg (6.1 kPa); the FiO<sub>2</sub> was set to 0.55. Likewise, the norepinephrine application was reduced within an hour to 0.35 µg/kg/min. Within the subsequent 24h, there were three massive episodes of hemodynamic instability requiring cardiopulmonary resuscitation, which evoked the clinical suspicion of a possible pulmonary embolism. The concentration of D-dimers was only slightly elevated at 0.35 mg/L. The patient's clinical status did not, however, permit transport for imaging diagnostics, so a transesophageal echocardiography was performed. No intracardial clots or valve vegetations could be found as a possible embolism focus. A slight right-left shunt via a persistent Foramen ovale could be demonstrated as a sign of pulmonary hypertension. With the working diagnosis of recurrent pulmonary embolism and contraindicated thrombolysis, the patient was given conservative therapy with PTT-controlled heparinization.

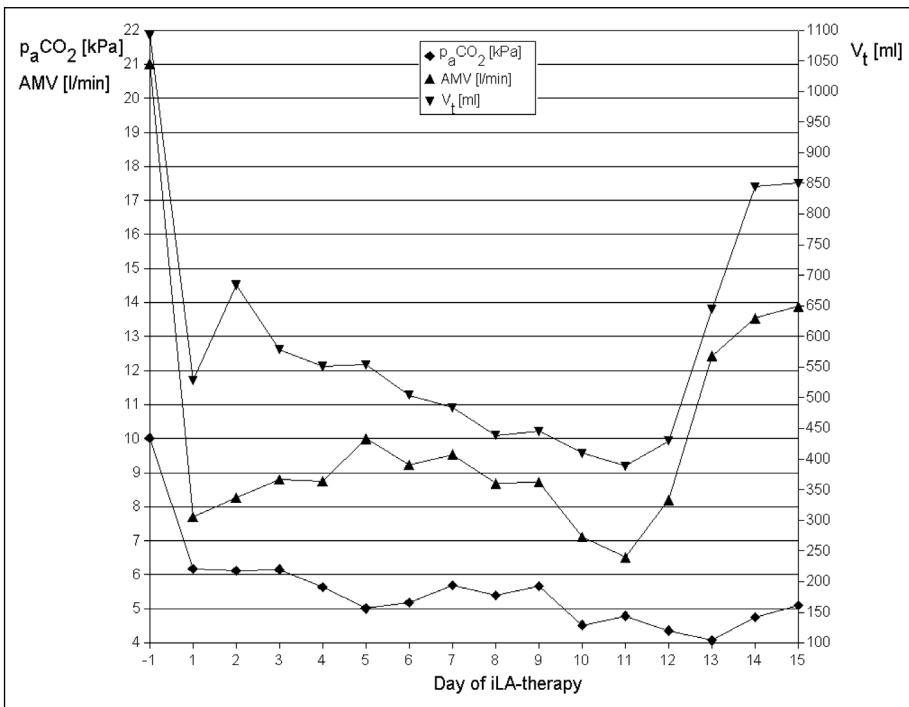


Figure 1. 24-h mean values of selected ventilation-associated parameters.

Note the changes from day -1 (pre iLA) to day 1 (start iLA) and after day 13 (tapering of treatment)

Overall, clear stabilization could be attained over the following 72h under the continued sepsis therapy and pECLA [CRP 60.3 mg/L; PCT 1.01 ng/mL; leukocytes 28.6 Gpt/L; norepinephrine 0.1  $\mu\text{g}/\text{kg}/\text{min}$ ;  $p_{\text{max}}$  25 mbar;  $V_t$  0.44 L;  $\text{FiO}_2$  0.6;  $p\text{CO}_2$  4.36 kPa (32.7 mmHg)], so that CT diagnostics could be performed on the 11<sup>th</sup> day of treatment. The CT showed commenced healing of the abscess changes in the throat and upper mediastinum. Moreover, dye recesses were conspicuous in the main trunk of the right pulmonary artery and the lower lobe branch of the left pulmonary artery in the sense of previous pulmonary embolism. The search for the source of embolism and for coagulation disorders was unsuccessful.

The pECLA therapy could be tapered off between the 13<sup>th</sup> and 15<sup>th</sup> day. Reduction of the gas flow via the pECLA required adjustment of the alveolar ventilation (Figure 1). The patient could finally be weaned from the respirator and transferred to a rehabilitation facility after 72 days in intensive care.

## Discussion

This case report describes the use of a pumpless arteriovenous system for extracorporeal  $\text{CO}_2$  elimination („pumpless extracorporeal lung assist, pECLA“) in a

patient with severe sepsis following primary odontogenic throat abscess with descending mediastinitis. Realizing the complexity of this clinical presentation, the focus of this discussion is placed on the extracorporeal  $\text{CO}_2$  elimination.

pECLA therapy was applied as ultima ratio to stabilize the patient. Analogous to ECMO, “rapid” and “slow” inclusion criteria were defined for indication of pECLA use. “Rapid” inclusion criteria are acute, serious pulmonary damage ( $\text{paO}_2/\text{FiO}_2 < 80$  mmHg and/or  $\text{paCO}_2 > 70$  mmHg under optimized conservative therapy), “slow” inclusion criteria a subacute serious limitation of oxygenation and/or  $\text{CO}_2$ -elimination ( $\text{paO}_2/\text{FiO}_2 < 150$  mmHg,  $\text{paCO}_2 > 60$  mmHg under optimized therapy for  $> 48\text{h}$ ) [11].

With correction of the respiratory acidosis after connecting the pECLA (corresponds to „slow“ inclusion criteria) the catecholamine dose, apart from the CPR, could be clearly reduced. This, like the high effectiveness of the extracorporeal  $\text{CO}_2$  elimination (Figure 1) which we observed, corresponds to the results published by other teams [8, 9, 10, 11]. Adequate blood flow of  $> 1.5$  L/min via the membrane lung is prerequisite to the proper function of the unit. For this reason, there should be a MAP  $> 70$  mmHg [8] or a cardiac index  $> 3$  L/min/m<sup>2</sup> [9]. Septic shock is generally considered being a contraindication to the use of a

pECLA for this reason, since systemic vascular resistance is additionally reduced and adequate blood flow via the membrane lung cannot be guaranteed, or the microcirculation deteriorates further.

In an animal model, Brunston et al. found a decrease in organ blood flow during arteriovenous carbon dioxide removal of about 10-20% at a shunt of 5-25% of cardiac output (CO). This was well tolerated by the animals without hemodynamic instability or organ failure due to hypoperfusion (5).

As mentioned above, the pECLA was the last therapeutic option, and the patient must be considered being in septic shock (proven infection, pulmonary dysfunction, vasopressor support). Remarkably neither the blood flow through the pECLA device nor the cardiopulmonary stability under pECLA seemed to suffer from this fact, which means that we used this device successfully in septic shock. We also did not find elevated lactate levels indicating deterioration of microcirculation (pre pECLA: 1.7 mmol/L, during pECLA 1.4-2.5 mmol/L, CPR up to 7.53 mmol/L). Maybe the pECLA's alteration of the circulatory system was not grave enough to cause major impairment to hemodynamics (Shunt < 25% of CO). Another explanation may be that the attenuation of the acidosis restored the organism's response to sympathomimetic amines and thus compensated the pECLA's effects on the systemic vascular resistance.

Prognostic statements cannot yet be made concerning the use of extracorporeal CO<sub>2</sub> elimination. Preliminary results show high effectiveness of the procedure and a reduction of the side effects of "lung-protective ventilation" [8, 10].

## Conclusion

The pECLA device proves to be highly efficient in CO<sub>2</sub>-removal. This way we were able to recompensate

the therapy-resistant respiratory acidosis which resulted from pneumonia and septic shock. Hemodynamic stabilization could be achieved despite the fact that the patient was in septic shock. Further reports will have to show whether this is coincidence or not.

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