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PRACTICAL PEARL

Apnea Test for Brain Death Determination in a Patient on Extracorporeal Membrane Oxygenation

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Abstract
Background Apnea test is a key component to confirm brain death. For patients receiving extracorporeal membrane oxygenation (ECMO), apnea test remains challenging. Brain death (BD) diagnosis is often made without apnea test.
Case We report the case of a 29-year-old man presenting clinical signs of BD while treated with ECMO therapy for refractory cardiogenic shock. Decreasing the ECMO sweep gas flow from 3 to 1 L/min and increasing oxygen delivery to 100 % on ECMO during the apnea test have allowed increasing the $PaCO_2$ of more than 20 mmHg without decreasing PaO_2.
Discussion In order to diagnose BD, neurological examination should be complete, including apnea testing, which can be not possible in patients receiving ECMO due to CO_2 removal from the membrane. Decreasing sweep gas rate allows reduction in CO_2 diffusion through the membrane. However, decreasing the ECMO gas flow to zero could be insufficient to maintain normoxemia. Decreasing (but not stopping) the sweep gas flow to 1 L/min and increasing the oxygen delivery through the ECMO have allowed performing the apnea test safely.
Conclusion To assess brain death in patients on ECMO, apnea test can be performed without compromising oxygenation by decreasing (but not stopping) the sweep gas flow and increasing oxygen delivery through the membrane.

Keywords Brain death · Extracorporeal membrane oxygenation · Apnea test · Sweep gas · Coma

Introduction

Extracorporeal membrane oxygenation (ECMO) is a bedside modified heart–lung machine, used to support acute, severe and reversible cardiac and/or pulmonary failure. It has been successfully used in various causes of cardiac failure [1]. Nevertheless, ECMO is associated with a high rate of deaths and neurological injuries [2]. Thiagarajan et al. [3] reported an incidence of 21 % of brain death (BD) associated with ECMO therapy. Due to carbon dioxide (CO_2) removal from the membrane, BD diagnosis, and especially apnea test, remains challenging in patients receiving ECMO [4].

Case

A 29-year-old male has been admitted in our hospital for chest pain with signs of acute non-ST-elevation myocardial infarction. The echocardiogram revealed a severe aortic stenosis linked to a bicuspid valve. The patient experienced a third degree atrioventricular block followed by a ventricular fibrillation, treated with electrical cardioversion

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and epinephrine for a total of 50 min of cardiopulmonary resuscitation. A veno-arterial ECMO was placed to assist the refractory cardiogenic shock, and the aortic valve was surgically replaced in emergency. The patient was afterward admitted in the intensive care unit under sedation (propofol 80 mg/h) and mechanical ventilation.

On day one after surgery, a bilateral mydriasis associated with Glasgow coma score at 3 and diabetes insipidus appeared. Propofol was stopped for neurological assessment. The neurological examination found a coma with absence of brainstem response. Brain CT scan was not possible due to his clinical condition. A first electroencephalogram was performed revealing persistent low-voltage frontal activity. A repeat neurological examination was performed 6 h later. The patient was still unresponsive with absence of brainstem responses.

In order to assess brain death diagnosis, an apnea test was performed. Before starting the apnea test, body temperature was 36.5 °C, mean arterial pressure (MAP) 70 mmHg, heart rate 100 bpm with norepinephrine infusion at 2.2 mg/h and epinephrine at 0.4 mg/h. ECMO parameters were ECMO blood flow = 4.1 L/min; inspired fraction of O_2 (FiO_2) = 40 %; sweep gas flow = 3 L/min. Mechanical ventilation parameters were tidal volume = 580 mL, respiratory rate = 16, FiO_2 = 21 % and positive end expiratory pressure = 6 cmH_2O. FiO_2 was increased to 100 % on ECMO, whereas FiO_2 was kept at 21 % on the ventilator. After 10 min of preoxygenation, on initial arterial blood gas analysis, arterial partial pressure of oxygen (PaO_2) was 256 mmHg, arterial partial pressure of carbon dioxide ($PaCO_2$) 47 mmHg and pH 7.43. Mechanical ventilation was interrupted, and a T-piece oxygen delivery at 9 L/min was connected to the tracheal tube. In the same time, sweep gas flow was decreased from 3 L/min to 1 L/min. During this 10 min apnea test, respiratory movements were absent, hemodynamic parameters were stable and catecholamine infusions remained unchanged; after 10 min of apnea test, arterial blood gas revealed a PaO_2 of 353 mmHg, $PaCO_2$ of 67 mmHg and pH of 7.28. The apnea test was considered as positive, and the mechanical ventilation was restarted. BD was confirmed by two electroencephalograms as required by the French law, but the organ donation was refused by the family.

Discussion

Clinical assessment of brain death is made on several criteria: irreversible coma with a known cause, loss of brainstem reflexes and positive apnea testing [5]. Prerequisites include the absence of cerebral nervous system-depressant drugs or neuromuscular blocking agents; no severe electrolyte, acid–base or endocrine disturbances; achievement of a normal core temperature (>36 °C) and a normal systolic blood pressure (>100 mmHg) [6]. In France, a confirmatory test must afterward be performed. Legal ancillary tests include cerebral angiography, computed tomography angiography or two electroencephalograms performed with a 4 h interval [7]. Nevertheless, BD is first a clinical diagnosis, and apnea testing should be performed.

In veno-arterial ECMO, blood is drained from a venous cannula placed near the right atrium and returned to a femoral arterial cannula. The external circuit carries venous blood to the membrane oxygenator, an artificial lung, to increase O_2 and remove CO_2, before reinjection. CO_2 clearance depends on the rate of sweep gas flow through the oxygenator, on the ECMO blood flow, on the physical properties of the oxygenator (maximum CO_2 exchange rate) and on the presence of CO_2 in the inspired gas. In case of low sweep gas flow, if the other parameters are stable, CO_2 removal is mainly dependent of the rate of sweep gas flow through the oxygenator [8].

Various techniques have been used for apnea tests [6]. We used the apneic oxygenation–diffusion with a T-piece oxygen delivery at 9 L/min, with respect of prerequisites (normotension, normothermia, euvolemia and absence of hypoxia) [6]. A moderate hypercapnia was present at baseline, which could have had been corrected by increasing sweep gas flow on ECMO (for an ECMO blood flow of 4 L/min, a sweep gas flow of 4 L/min should have been better to obtain a normocapnia). Apneic oxygenation–diffusion has been proven to be safe [9], even if respiratory acidosis and hypercarbia linked to apnea testing may be associated with cardiac arrhythmias or hypotension [5].

Apnea testing is considered positive if respiratory movements are absent, and $PaCO_2$ is above or equal to 60 mmHg or increases for at least 20 mmHg [6]. In order to limit CO_2 removal from the ECMO, the sweep gas flow has been decreased from 3 to 1 L/min. Decreasing sweep gas rate allows reduction in CO_2 diffusion through the membrane. If the sweep gas rate is maintained at the same level, the interruption of mechanical ventilation is not sufficient to provide an increase in $PaCO_2$. Yang et al. [11] proposed to turn the ECMO gas flow to zero during the apnea test. However, it could be insufficient to maintain normoxemia [4]. The use of a continuous positive airway pressure (CPAP) has been shown to be prevent hypoxemia [10]; In our case, the observed increase in PaO_2 during apnea is probably related to the increased oxygen delivery through the ECMO, but also the result of maintaining (and not stopping) a sweep gas flow. We selected 1 L/min of sweep gas flow during apnea testing as an estimation of the best level between blood oxygenation and CO_2 clearance for this patient.

In case of hypothermia, a lower sweep gas flow would probably be required to allow CO_2 to rise because of reduced body metabolism and CO_2 production. In the same way, hypotension would probably require a reduced gas flow. Morphologic parameters and gender also influence basal metabolism rate and CO_2 production, but probably without enough differences to affect the required sweep gas flow.

Conclusion

Assessment of BD, especially apnea test, remains challenging in patients receiving ECMO. Here, we describe a simple and safe method of apnea testing in a patient on ECMO. Decreasing the sweep gas flow to 1 L/min and increasing oxygen delivery to 100 % on ECMO during the apnea test have allowed to significantly increase the $PaCO_2$, and to conclude to a positive apnea test, without compromising oxygenation.

Conflict of interests The authors have not disclosed any potential conflicts of interests.

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