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Cerebral hemodynamics monitoring during extracorporeal membrane oxygenation in piglets

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ABSTRACT

Critically ill neonates are subjected to severe and abrupt hemodynamic imbalances that could cause cerebral damage (e.g., hemorrhage, ischemic events). In this population, the need for cerebral monitoring tools to identify dangerous hemodynamic variations in real-time is paramount. Near-infrared spectroscopy (NIRS) is largely exploited in neonatal intensive care units (NICU) to monitor critically ill patients' cerebral oxygenation. However, the most used NIRS devices exploit continuous wave NIRS (CW NIRS) technique, which is affected by motion artifacts and has low penetration depth compared to other more complex NIRS techniques. Moreover, CW-NIRS does not allow the investigation of tissue perfusion. Thus, in this ongoing study, we tested a hybrid device that combines time-domain NIRS (TD-NIRS) and diffuse correlation spectroscopy (DCS) for monitoring absolute cerebral total hemoglobin concentration (tHb), cerebral tissue oxygen saturation (S_tO_2), and cerebral blood flow index (BFI) of piglets during induced hemodynamic variations. Cerebral hemodynamic variations were induced during extracorporeal membrane oxygenation (ECMO) procedure, simulating four common conditions affecting the cerebral hemodynamics of ill neonates: hypocapnia, hypercapnia, hypotension, and hypertension. We measured 4 piglets, and the preliminary results shown in this study are promising, obtaining hemodynamic variations in accordance with previous findings, and empowering the possibility to exploit hybrid TD-NIRS and DCS devices to assess cerebral health of ill neonates.

Keywords: cerebral hemodynamics, time-domain NIRS, diffuse correlation spectroscopy, ECMO, piglets

1. INTRODUCTION

About 5-10% of preterm neonates suffer from neurological damage, such as cerebral palsy, and 20-25% of them are affected by the minor neurocognitive disease [1]. Indeed, common pathologies in preterm neonates are acute respiratory distress syndrome and damages in cerebral autoregulation that leave the brain exposed to strong variations in hemodynamics and could lead to hypoxia, hypoperfusion, or ischemia. Extracorporeal Membrane Oxygenation (ECMO) is a lifesaving procedure for patients with respiratory and cardiovascular failure refractory to conventional therapies. Although ECMO technology and expertise have increased over the years, the procedure is still associated with complications, affecting short- and long-term outcomes, such as neurological complications. Furthermore, patients requiring ECMO are exposed to hypoxia and acidosis periods caused by underlying diseases that could increase the risk of neurological damage [3]. Since there are no therapies to reduce cerebral damage other than preventive strategies, cerebral monitoring is paramount. NIRS has already been exploited during ECMO for monitoring cerebral oxygenation variations [4]. This study tests a hybrid device that combines TD-NIRS and DCS by measuring piglets' cerebral hemodynamic variations during ECMO. The aim of the study is to validate the ability of hybrid devices in monitoring cerebral health to exploit it in clinical practice for neonatal neuro-monitoring.

2. MATERIALS AND METHODS

The experiments were conducted on 10-day-old Large White pigs (n = 4) weighing between 4 and 6 kg. All animal procedures were carried out in accordance with the national and European legislative and administrative provisions in force. The study protocol was approved by the animal welfare body (OPBA) of the Università degli Studi di Milano and by the Italian Ministry of Health (authorization number 531/2020 PR). The piglets were sedated by an intramuscular (i.m.) administration of medetomidine (0.025 mg/kg) and tiletamine/zolazepam (5 mg/kg) and underwent surgery to be supported by venous arterial (VA) ECMO by cannulation of the external jugular vein and right carotid artery. Vital parameters were continuously recorded during the procedure. After about one hour from the end of the surgery, and when stable vital and hemodynamic parameters were reached, four protocols were performed in the following order:

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hypocapnia, hypercapnia, hypotension, and hypertension. The probe of the hybrid device was positioned on the head of the piglets, far from synovial cavities, and the inter-fiber distances were 2.5 cm for the TD-NIRS module and 2 cm for the DCS module. Indeed, the skull thicknesses of neonatal piglets are very small (generally less than a few millimeters), which guarantees a high sensitivity to brain tissue with both modules. Simultaneous acquisitions of 1s integration time were performed with both modules.

Hypocapnia and hypercapnia were induced by changing the sweep gas in the ECMO circuit to modify the CO_2 level from the normal range. During hypocapnia (hypercapnia), the sweep gas is increased (reduced) gradually until the CO_2 level reaches 20 mmHg (80 mmHg). The protocol consists of 10 (or more) min of baseline, with stable hemodynamic parameters and level of $paCO_2$ within 40-50 mmHg; then hypocapnia (hypercapnia) is induced by increasing (reducing) the sweep gas; and finally, another 10 min of recovery ($paCO_2$ return to normal values). Hypercapnia was also simulated by the direct introduction of CO_2 into the ECMO circuit via a CO2 bottle instead of reducing the sweep gas to induce faster hemodynamic variations.

Hypotension and hypertension were induced by intravenous administration of sodium nitroprusside and noradrenaline, respectively. Sodium nitroprusside is a direct-acting vasodilator agent, generally used to rapidly reduce blood pressure; noradrenaline, on the other hand, is a vasopressor agent, generally used to increase blood pressure. The protocol consists of 10 min (or more) of baseline, with stable value for the mean arterial blood pressure (MABP); then hypotension (hypertension) is induced, reducing (increasing) the MABP of 30%; and after 10 minutes of hypotension (hypertension), MABP is increased (reduced) to its normal values.

3. RESULTS AND DISCUSSION

We enrolled 4 piglets, and in Fig. 1, we reported the hemodynamic variations measured for one piglet during hypotension (panels a), b), and c)) and hypercapnia (panels d), e), f)) protocols.

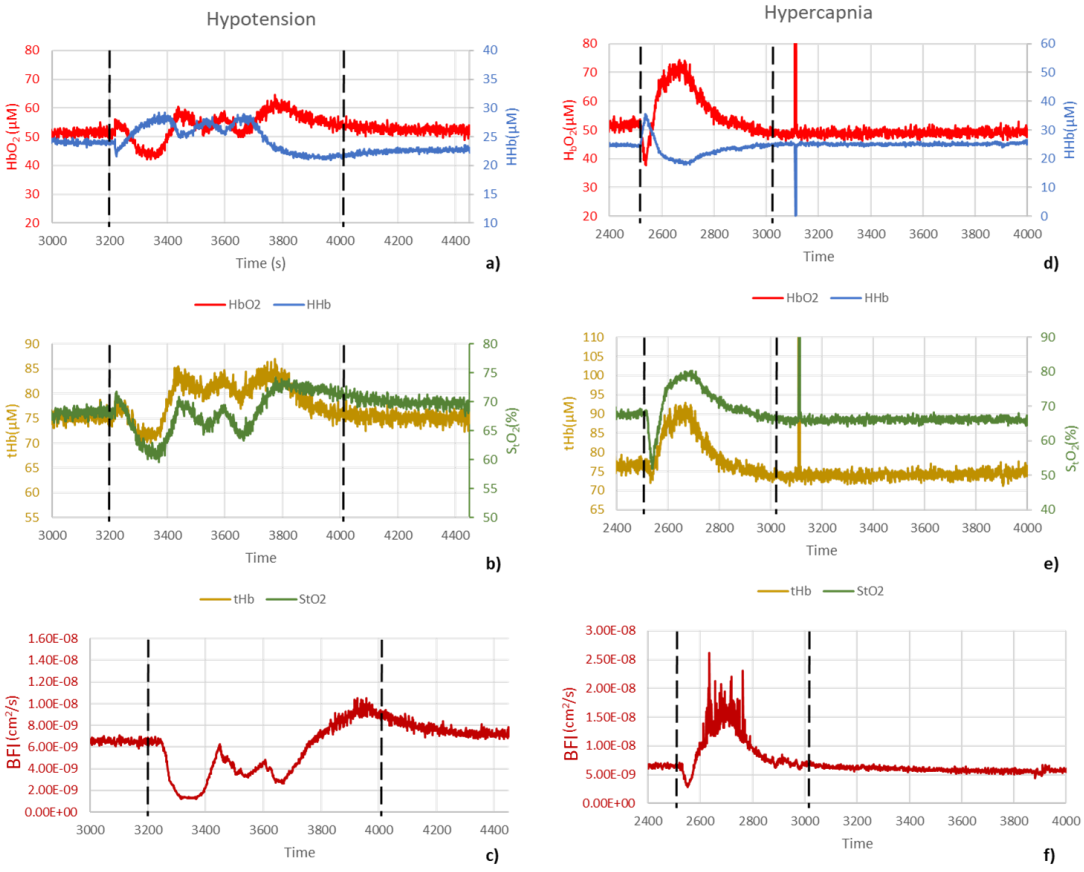

Figure 1. Hemodynamic variations during hypotension (on the left) and hypercapnia (on the right). Panels a) and d) oxygenated (HbO_2) and deoxygenated (HHb) hemoglobin; panels b) and e) tHb and S_tO_2; panels c) and f) blood flow index (BFI); black dashed lines represent the start and the end of the protocols (hypotension on the left and hypercapnia on the right).

Similar results have also been obtained for the other piglets. Observed variations are in accordance with literature: reduction in cerebral S_tO_2 and BFI in case of hypotension [5,6] and increase of cerebral S_tO_2 and BFI in case of hypercapnia [7,8].

4. CONCLUSIONS

Four piglets were monitored during ECMO with a hybrid diffuse optics device. The absolute concentration of oxygenated, deoxygenated, and total hemoglobin and blood flow were measured during real-life hemodynamic variation (hypotension, hypertension, hypocapnia, hypercapnia), and retrieved results are in accordance with previous findings. During the protocols, a commercial CW-NIRS device was exploited to compare the oxygenation level measured. Other than that, many sensors were used to monitor the piglet health (i.e., mean arterial pressure, arterial saturation); we are working to combine information measured from all the sensors and enroll more piglets in the study to reinforce the statistic of our promising results.

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