Interference between cerebral NIRS and conjugated bilirubin in extremely low birth weight neonates☆

Interferencia entre NIRS cerebral y bilirrubina conjugada en neonatos de extremado bajo peso

To the editor:

Near-infrared spectroscopy (NIRS) is becoming a widespread method for monitoring of ill infants in neonatal intensive care units. The detection by NIRS of cerebral hypoxia in extremely preterm newborn infants and its correction with appropriate care measures decreases the time spent in hypoxia by the immature brain, although the evidence on the impact of NIRS monitoring on long-term neurodevelopmental outcomes is still not robust.[1] Studies in adult patients with liver disease show that high levels of bilirubin may interfere significantly with cerebral NIRS monitoring, but this phenomenon has not been investigated in neonates.[2–4] We present 4 cases of interference with NIRS monitoring in extremely low birth weight (ELBW) infants with conjugated hyperbilirubinaemia.

The ethics committee of our hospital approved the retrospective analysis as exempted it from the need to obtain informed consent. The patients were ELBW neonates born between 25^{+0} and 28^{+5} weeks of gestation with birth weights of 500 to 990 g who developed multifactorial cholestasis with progressive elevation of serum conjugated bilirubin. Concurrent to this process, we observed a reduction in the cerebral regional oxygen saturation (rSO_2) measured by NIRS. Table 1 presents the clinical characteristics of the patients and Table 2 the changes over time in the levels of bilirubin and cerebral rSO_2 measured by NIRS. In these 4 patients, the abnormal NIRS values could not be explained by abnormalities in haemoglobin concentration, partial pressure of CO_2, oxygen saturation ($SatO_2$), lactate levels or blood pressure. In every case, an ultrasound examination confirmed that cerebral blood flow (CBF) velocities and cardiac output were normal. In patients A and D, once they were stable and cholestasis had resolved (at 33 days and 4 months of age, respectively), NIRS monitoring was resumed and detected normal values.

These 4 ELBW infants with multifactorial cholestatic hyperbilirubinaemia had rSO_2 values indicative of risk of severe cerebral hypoxia, but after the common causes of altered cerebral NIRS monitoring values were ruled out, this finding was attributed to hyperbilirubinaemia.[1] Although cerebral rSO_2 decreases progressively in the first days of life in preterm infants, the values observed in our patients were below those reported in the literature and therefore were not completely explained by this pattern. In addition, in patients A and D, the rSO_2 normalized as the hyperbilirubinaemia improved. To our knowledge, no evidence on this phenomenon has been published for the neonatal population, but studies in adults with liver disease have reported a negative correlation between the cerebral rSO_2 and the serum bilirubin level.[2,4] Furthermore, some authors found that NIRS was not at all reliable in patients with severe hyperbilirubinaemia during liver transplantation.[3] The products of the degradation of the haem group are chromophores that absorb light in the near-infrared range (650-900 nm), but do not modify cerebral blood flow or oxygen uptake. Therefore, the interaction between bilirubin levels and rSO_2 has been attributed to a competitive absorbtion of light by bilirubin and haemoglobin.[2,4] There is solid evidence on the interference between haemoglobin and bilirubin in the measurement of bilirubin levels by transcutaneous or spectrophotometric methods in newborn infants, a problem that can be bypassed by the simultaneous measurement of several wavelengths. Interestingly, the use of NIRS in stool samples has been investigated as a means to detect biliary atresia in neonates.[5] In patients with this condition, the absorbance peak at 730 nm attributed to conjugated bilirubin is absent, contrary to the samples of patients without biliary atresia. The evidence shows that the presence of meconium in the bowel, with its high concentration of conjugated bilirubin, interferes with abdominal NIRS monitoring using most of the devices currently available.[6] For this reason, clinical trials are currently underway to test NIRS systems that include algorithms to compensate for the presence of meconium in the bowel. Monitors made by different manufacturers use different wavelengths, and therefore the interference of bilirubin may vary between systems, but this aspect has also not been studied to date.

It would be interesting to investigate whether unconjugated and conjugated bilirubin interfere with NIRS monitoring to the same extent, given the high incidence of indirect hyperbilirubinaemia in neonates.

In short, this case series suggests that hyperbilirubinemia may interfere with NIRS monitoring in VLBW infants. Large-scale, robust studies are required to corroborate these findings and to explore relevant questions, such as the role of indirect bilirubin in this interference and whether NIRS values are associated with the degree of hyperbilirubinaemia. Our findings warn of the limitations of NIRS in detecting changes during regional monitoring in this group of patients.

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Table 1 Clinical characteristics of the patients.

	Sex	Weeks of gestation	Birth weight	History	Main problems	Outcome
Patient A	Male	25^{+1}	500 g	Maternal preeclampsia Caesarean delivery	RDS, hypotension	Discharge home
Patient B	Female	27^{+1}	800 g	Maternal preeclampsia and HELLP syndrome Caesarean delivery	RDS, PDA, PH, NEC	Death
Patient C	Male	25	700 g	Maternal preeclampsia and HELLP syndrome Caesarean delivery	RDS, PH, grade III IVH, hydrocephalus, NEC	Death
Patient D	Male	28^{+5}	990 g	Twin pregnancy Caesarean delivery	Late-onset sepsis, mild BPD, grade II IVH	Discharge home

BPD, bronchopulmonary dysplasia; HELLP, haemolysis, elevated liver enzymes and low platelet; IVH, intraventricular haemorrhage; NEC, necrotising enterocolitis; PDA, patent ductus arteriosus; PH, pulmonary hypertension; RDS, respiratory distress syndrome.

Table 2 Temporal trends in bilirubin and cerebral rSO_2.

Patient A	Days post birth	3	4	5	6	7	33
	$CrSO_2$ (%)*	79	67	62	46	44	65
	Bilirubin: conjugated/total (mg/dL)	1.86/7.3	2.94/8.4	5.1/8.1	5.88/8.7	7.86/10.7	0.8/0.8
Patient B	Days post birth	3	6	12	17		
	$CrSO_2$ (%)*	73	72	68	55		
	Bilirubin: conjugated/total (mg/dL)	0.66/6.7	1.47/6.7	2.71/4.5	3.45/5.3		
Patient C	Days post birth	3	6	9	11	13	
	$CrSO_2$ (%)*	65	63	48	44	41	
	Bilirubin: conjugated/total (mg/dL)	0.9/7.0	1.26/4.5	3.29/5.2	8.63/12.7	21.65/25.9	
Patient D	Days post birth	3	16	19	81	111	
	$CrSO_2$ (%)*	77	62	54	63	66	
	Bilirubin: conjugated/total (mg/dL)	0.57/11.1	5.21/8.4	6.69/10.5	2.64/4.5	1.97/3.3	

$CrSO_2$, cerebral regional oxygen saturation.
* Data recorded hourly in patient charts at the time of blood sampling (INVOS 5100 C, Covidien, Mansfield, MA, USA) (neonatal OxyAlert NIRSensor, Mansfield MA, USA).

Conflicts of interest

The authors have no conflicts of interest to declare.

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Simulation during COVID-19 pandemic in the Spanish pediatric intensive care units: New challenges in medical education☆

Uso de la simulación durante la pandemia COVID-19 en las UCIP españolas. Nuevos retos en educación médica

Dear Editor:

Simulation-based medical education, which allows clinicians to develop skills to manage serious and infrequent situations without detriment of patient safety,[1] is even more important during unexpected public health emergencies like the pandemic we are currently experiencing.[2]

The coronavirus disease 2019 (COVID-19) pandemic has brought on numerous adjustments that have limited the pursuit of medical education activities,[3] including the development of simulation programmes. Therefore, we need to contemplate the development of other modalities of simulation, such as remote simulation, to substitute or supplement in situ simulation training to be able to continue implementing educational programmes.[4–6]

We present the results of a cross-sectional, observational survey-based study aimed at assessing the use of simulation for preparing clinicians to manage COVID-19 during the first and second waves of the pandemic at paediatric intensive care units in Spain, as well as the the simulation modalities used, and the continuation of simulation activities unrelated to COVID-19.

Nineteen Spanish paediatric intensive care units (PICUs) of different levels of care (Appendix A) submitted responses to the survey in December 2020. Ten of these units had simulation training programmes as part of their regular educational curriculum prior to the COVID-19 pandemic. More than half started implementing the COVID-19 trainings in March 2020, 8 were able to start the trainings before starting to manage COVID-19 patients, 2 started the trainings at the same time they started managing patients, and 9 after starting to manage patients. In 9 PICUs, the COVID-19 training programme was an initiative of the unit itself.

Table 1 presents the equipment and technology available to the units to deliver the training programmes, with a predominance of low-cost equipment. Only 2 units had access to the technological resources required to offer remote simulation, and none had access to virtual reality simulators.

The scenario covered most frequently in these trainings was the correct donning and doffing of personal protection equipment (PPE), followed by airway management and cardiopulmonary resuscitation (CPR) (Table 1). Most trainings were conducted in situ (in the patient care setting): 73.7% of trainings on the donning of PPE, 57.1% of trainings on airway management, 61.5% of CPR trainings and 63.6% of trainings on other scenarios. Less frequently, simulation trainings were delivered outside the unit in specific facilities or centres. A substantial proportion of units (13/19) delivered multidisciplinary trainings and 12/19 of the units included other departments in their training programme.

Table 1 presents the barriers identified by participating units in delivering the trainings, with a high percentage reporting logistic problems, a lack of time and a lack of staff. Have the units reported lack of previous training and concerns regarding infection. Social distancing measures affected training programmes in nearly 60% of units, and the lack of alternatives like remote simulation was another of the identified barriers. Units also frequently reported problems related to material resources and funding.

The main problems reported by participants regarding group dynamics were difficulty communicating due to wearing PPE in 12 of the 19 units, anxiety or concerns in the care team in 12, lack of knowledge of COVID-19 care practices in 9 and lack of knowledge of COVID-19 teamwork in 8. Compared to simulation-based training programmes offered prior to COVID-19, engagement of the team in trainings during the pandemic was the same in 9 of the units and greater in 7.

When it came to the continuation of simulation-based activities unrelated to COVID-19, 14 of the 19 units continued implementing simulation-based activities, although less frequently and with fewer participants. Only 5 of the units were able to continue the regular simulation-based training programme without significant adjustments. Only 3 units used remote simulation to offer simulation-based trainings unrelated to COVID-19.

Participants considered the training programme useful to improve the management of patients with COVID-19 (Table 2).

Despite the potential limitations of the study, including the subjectivity of survey-based designs and that responses were only submitted by half of the PICUs in Spain, it reflects the use of simulation in this care setting during the COVID-19 pandemic. Simulation has been used to train in different scenarios related to COVID-19, mainly with low-cost technology and in situ trainings. Emerging modalities like remote simulation[3,4] using different applications, including some inexpensive options,[5–7] are still rarely used by Spanish PICUs. Despite the reported barriers, participants found the training programmes very useful.

Simulation-based medical education must be established as part of the regular training curriculum of all units deliver-

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