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EDITORIAL

Neuroprotection for asphyxiated neonates in settings with limited resources

El cuidado del cerebro del neonato asfixiado en entornos con recursos limitados

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In recent decades, we have witnessed enormous advances in the knowledge of the pathophysiological mechanisms of hypoxic-ischaemic encephalopathy (HIE) in newborns and numerous clinical trials were performed that identified therapeutic hypothermia (TH) as the only evidence-based intervention effective in partially reducing the high morbidity and mortality associated with this condition. However, asphyxia still remains the third leading cause of neonatal death globally, chiefly on account of infants born in low- and middle-income countries, where 96% of cases of encephalopathy associated with perinatal events take place.[1]

In 2021, the HELIX clinical trial (''hypothermia for encephalopathy in low- and middle-income countries''), conducted in 3 countries in South Asia, found that management with TH increased the mortality of asphyxiated babies and its results made us reflect whether what is good for some may not be good for all, highlighting the importance of the differences between population in the development and outcomes of brain injury.[2] These factors affect maternal health, limit access to prenatal care and are associated with an increased frequency of out-of-hospital births and infection, variables that in turn affect the incidence, course and outcomes of HIE. On the other hand, while TH has proven effective for specific conditions, the incidence of cerebral palsy, intellectual disability and behavioural disorders after its use in HIE continues to be high,[3] which reminds us that additional interventions are required to minimise brain injury and improve outcomes in affected infants.

In Peru, the only experience in the application of high-technology TH started 6 years ago at the Instituto Materno Perinatal de Lima, a public teaching hospital that has 3 intensive care units, staff dedicated to neonatal neurologic care, continuous electrocardiographic and electroencephalographic monitoring equipment, neuroimaging equipment and a programme for the follow-up of high-risk patients through age 5 years. These conditions have allowed delivery of TH in adherence with international guidelines and with favourable outcomes.[4] However, circumstances in Peru, as in many other Latin American countries, are quite heterogeneous. In Lima, besides the aforementioned institute, only a few private hospitals can offer cooling. In the rest of the country, it is not available. This means that the vast majority of infants with neonatal asphyxia will not have access to this treatment option. Peru, which has an extensive territory and a complex geography, does not have effective patient transport systems. The quality of perinatal care is highly variable and health care budgets can change from one year to the next depending on the current government. There is very little investment in research and data

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registering is scarce. For these reasons, TH in Peru, be it high- or low-tech, has yet to be implemented on a large scale. This also seems to be the status quo in other countries in the region. A study by the SIBEN neonatal network, which collects data from 35 neonatal intensive care units in Latin America, found that barely 13% of newborns with moderate to severe HIE could access this treatment in 2019.[5] These circumstances compel us to reconsider the underlying issue: the universal and basic management of the first hours post birth in asphyxiated newborns with HIE, regardless of the setting. Greater emphasis should be placed on this in resource-limited settings, and not necessarily on the delivery of TH. In this context, we consider that the publication of evidence-based recommendations aimed at these types of settings, such as those published by García et al. in the current issue of *Anales de Pediatría*,[6] fills a gap and responds to an urgent need, especially for health care professionals providing neonatal neurologic care in Latin America.

One of the most relevant aspects of the published recommendations is the authors' reminder of the urgent nature of interventions meant to preserve normal cerebral functioning and future healthy neurodevelopment in the infant. As is the case of other neurologic diseases, ''time is brain'' in this situation. The document offers a series of feasible recommendations, starting by underscoring the performance of neonatal resuscitation by qualified staff. The authors emphasise the care of the asphyxiated infant the first 6 h post birth, prioritising continuous monitoring of variables like central body temperature and blood glucose, care that ought to be delivered in a neonatal intensive care setting. A critical aspect on which there is wide consensus is the need to have specialists on staff with the necessary knowledge and skills to detect encephalopathy and assess it over time. This is essential for the classification of patients based on severity and for applying the various interventions required in their management and follow-up.

One of the most relevant publications for neonatal neurology in recent years is the document on the definition of neonatal seizures of the International League Against Epilepsy (ILAE) from 2021. It includes the routine use of encephalography (EEG) for diagnosis of seizures that may or may not have observable clinical features. The use of EEG is also recommended for the follow-up of patients with encephalopathy of different aetiologies and to determine the duration of treatment with antiepileptic drugs, suggestions that are particularly relevant for infants with HIE. In resource-limited settings, this new proposal further complicates the management of patients with seizures. The document addresses this challenge by recommending prophylaxis with phenobarbital in cases of moderate or severe HIE when there is a strong suspicion of clinical seizures and EEG equipment is not available. The current evidence supports this measure, although clinicians must consider the safety profile of the drug, the risk of toxicity with repeated administration and the total duration of treatment.

Some of the aspects on the management of HIE addressed in the recommendations are the knowledge of the differences between systemic and cerebral haemodynamics and the usefulness of imaging techniques such as sonography, which is inexpensive and widely available, not only to watch for the development of cerebral lesions and fluctuations in cerebral blood flow, but also for the evaluation of cardiovascular function. Some low-cost measures, such as trophic feeding, precise fluid management and close monitoring of electrolytes are easy to implement or reinforce and are supported by evidence.

A crucial but frequently neglected aspect is family-centred care. It is known that beyond the first days of life, the outcome of infants with HIE will depend largely on the environment where they grow up and are exposed to stimuli that foster their development. The document recommends family-centred care from the first hours post birth, offering emotional support and open communication and implementing measures that promote parent-child bonding in complex situations such as HIE.

The care of the neonatal brain poses an ongoing challenge and is a global responsibility. In resource-limited settings, HIE continues to be an important cause of mortality and disability. It is essential that evidence-based strategies continued to be pursued to standardise the basic and urgent care of all asphyxiated babies, regardless of where they are from.

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