

Neonatal Hypoxic-Ischemic Encephalopathy and Hypothermia Therapy: Solving Questions about Monitoring and Prognosis

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Abstract

Introduction: The hypoxic-ischemic encephalopathy is a significant cause of neurologic morbidity and mortality in the newborn. One of the standards of management is the hypothermia therapy that allows a reduction in the brain injury extension, making important to define the settings involving the admission to such therapy.

The hypothermia therapy protocol demands an strict compliance of the inclusion criteria, one of them, the APGAR score at a determinate moment, no protocol includes its score at different times, the APGAR score helps the clinician to decide the therapeutic approach of this patients, and the tenth minute score has received priority over the other minute's score, nevertheless many patients will lose the opportunity to be admitted for hypothermia therapy when this score is taken, although the ACOG has determined that it is the minute 5 APGAR that has the value to define neonatal asphyxia, most European and American protocols take the 10 minute APGAR score; besides it is possible that the newborn in the first 6 hours does not demonstrate the secondary damage, or energy failure that are generated up to 48 hours later, in which the use of hypothermia therapy has truly a therapeutic effect. Then it is imperative to analyze the early outcomes according to the APGAR in the minute 5 and 10 in patients admitted for hypothermia therapy.

Methods: A descriptive study, and retrospective analysis of a cohort of 62 patients born in term with hypoxic ischemic encephalopathy, admitted at the intensive care unit of Clinica Universitaria Bolivariana, Medellin, Colombia, between 2014-2016.

Results: The cohort of newborns exhibits a mortality of 8.1%, which was significantly associated with the presence of complications during hypothermia. The most frequent pattern found in the electroencephalographic line during the first day was suppression burst 45.2%, and heading to the end of the protocol, 51.6% achieved normalization; imaging findings such as the subcortical ischemia was the mostly found in 25.8%, but the hemorrhagic ones were only found in 12.9%. During a bivariate analysis a correlation between different outcomes were found, the most important of them, was the one among the presence of status during the electroencephalographic monitoring with an APGAR score under 5 at the fifth minute.

Conclusions: It is important to take on consideration the five-minute APGAR score because of its relation with epileptic status development, which in our cohort was more frequent without clinical manifestation than with it during monitoring. This is important because of the negative prognosis that this implies in the short term, in addition the patients that presented epileptic status post medication had correlation with persistent abnormalities at the discharge, that is why the five-minute APGAR score under five can predict the neurological examination at the discharge and the epileptic status development as a predictive marker. This also creates a suspect that the recommendation to use hypothermia therapy without electroencephalographic monitoring is a dangerous practice, and makes it difficult to assess the response to it.

Keywords: Newborn; Hypoxic-ischemic encephalopathy; Mortality; Neonatal seizures

Introduction

The ischemic hypoxic encephalopathy (HIE) is an entity produced as a consequence of a newborn's brain's oxygen supply reduction, preceded by hypoxemia or ischemia [1], being one of the main causes of alterations in the short, mid and long term in the neurodevelopment [2].

In our milieu, incidence and mortality of the condition are both unknown, but different studies show a 1.088 per 1,000 alive infants [3], furthermore a mortality that fluctuates between 13-15% [4,5] is reported, and up to a 10% death risk increase in patients with mild encephalopathy [2].

Different methods have been established for the entity handling. One of them is the cooling therapy, that initiated within the first 6 hours after birth and continued for 72 hours, allows to reduce the rate of death or moderate to severe disability in term newborns with HIE, reducing the cerebral lesion extension [2], and the development of chronic neurologic alterations with an NNT 7 [6]. For such therapy a

strict protocol is established, so patients' continuous monitoring and

	Sura 11 (17.7%)
	Coosalud 8 (12.9%)
	Coomeva 7 (11.3%)
	Media (SD)
Gestational age (Weeks) n=62	38,371 (1.333)
Weight (Kilograms) n=61	3,049 (0.421)
Size (Centimeters) n=36	49,666 (2,177)
Institutional delivery (At the Clinica Universitaria Bolivariana)	Yes 13 (21%)
	No 49 (79%)
Maternal delivery	Vaginal 34(54.8%)
	Cesarean 15 (24.2%)
	Vaginal+Forceps 9 (14%)
	Unknown 4 (6.5%)
Preeclampsia	Yes 2 (3.2%)
	No 58 (93.5%)
	Unknown 2 (3.2%)
Intra Uterine infection	Yes 4 (6.5%)
	No 56 (90.3%)
	Unknown 2 (3.2%)
Long labor final stage	Yes 21 (33.9%)
	No 41 (66.1%)
Umbilical cord prolapse	Yes 3 (4.8%)
	No 59 (95.2%)
Neck double Knot	Yes 7 (11.3%)
	No 55 (88.7%)
	Meconium I 2 (3.2%)
	Meconium II 4 (6.5%)
	Meconium III 1 (1.6%)
	Others 10 (16.1%)
	Normal 3 (4.8%)
Amniotic fluid characteristics	Unknown 42 (67.7%)

n (%)

Abnormal discontinuous: 13 (21%)

Suppression Burst: 28 (45.2%)

Wake up-sleep cycle: 2 (3.2%)

EEG pattern at day 1

Need of anticonvulsant drugs at hospital discharge	Clinical seizures	3.58 (1.12-11.34)	0.05
Needing of anticonvulsant drugs at hospital discharge	Post medication epileptic status	14 (1,96-126,56)	0.01
Epileptic status development	Tonic or clonic seizures	5.25 (1.17-23.78)	0.08
Epileptic status development	Sepsis	8.16 (1.18-71.17)	0.029
Status during electroencephalographic monitoring	Clonic seizures n=43	5.83 (1.27-26.93)	0.05
Status during electroencephalographic monitoring	APGAR score<5 at the fifth minute n=37	57 (1.06-33.6)	0.1
Status during electroencephalographic monitoring	APGAR score<5 at the tenth minute n=29	11.33 (1.91-67.78)	0.01

To sum up, we consider that the most relevant data is this study fully support the necessity that hypothermia therapy be spread around all neonatal units in the world, that can also count on the possibility of complexity monitoring, including the aEEG, and performing extension studies, besides the possibility of outpatient follow-up.

Conclusion

Nowadays HIE has an effective treatment and easy administration such as hypothermia therapy, but is necessary to count on enough technology to guarantee the aEEG monitoring during and after the therapy, because the events presented in this monitoring are most likely to be the principal prognosis markers. Additionally we left to readers' consideration the recommendation of using the 5 minute APGAR score better than the 10 minute score in the admission criteria for the therapy because of the important correlation between epileptic status development and the APGAR score aforementioned, being the epileptic status another marker for neurologic prognosis that can influence the hypothermia therapy.

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Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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