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Ischemic Hypoxia in Newborn Murine models: Main Clinical data

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Abstract

Neontal hypoxia is a pathology that currently generates important complications in patients. The time that elapses between the initial injury to the brain and the appearance of irreversible cellular damage due to ischemia and hypoxia varies considerably with the severity of the attack and the extent of the hypoxia. Currently the need to explore the different types of treatment for neonates is part of the basic research. The objective of this investigation was to identify the main characteristics of the murines after been submitted to hypoxia. **Material and method:** an experimental study will be carried out Wistar rats were submitted to hypoxia. **Results:** A total of 11 murines, after hypoxic stimulus, presenting lethargy in 81.8% of the cases, the neuromuscular strength remained without difficulty in 81.8%, and the walk showed difficulties in 100% of the cases. **Conclusion:** The most frequent lesions to assess for hypoxia in murines are damage to neurological function and musculoskeletal strength.

Introduction

Hypoxic-ischemic encephalopathy (HIE) is considered responsible of 23% of the 4 million neonatal deaths due to asphyxia. HIE occurs in 1-2 out of every 1000 term newborns, a significant portion dies or survives with severe long term aftermaths, 6-23% of the cases of cerebral palsy (CP) are due to intrapartum asphyxia (Al-Waili, N. S., Butler, G. J., Beale, J., Abdullah, M. S., Hamilton, R. W. B., Lee, B. Y, 2005; Secretaría de salud, 2010).

According to the World Health Organization the world rate of neonatal asphyxia is 10.8/1000 live newborns and it raises to 44.7% in newborns under 1,500 grams with a mortality rate close to 50%. (Secretaría de salud, 2010)

Ischemic encephalopathy is considered as a feature of the term newborns that will depend on the type and severity of injury and it will experience a severe lack of oxygen that causes a brain metabolism disruption. Global hypoxia is frequently followed by an extensive non-uniform ischemic injury due to apoptotic and necrotic cell death. (Lagercrantz, H. & Hanson, M.A. & Ment, L.R. & Peebles, D.M, 2010).

Newborns with HIE show anomalies in the brain energetic metabolism that is usual shortly after birth, but it shows a progressive decline in the phosphocreatin and inorganic phosphate ratio, besides the rise of lactate few hours later. Babies with this phenomenon develop severe neurogical impairment or die. Late decline of phosphocreatin and inorganic phosphate is closely related to brain growth reduction and the severity of neurodevelopmental impairment one and four years later. (Huchim O, 2017; Lagercrantz, H. & Hanson, M.A. & Ment, L.R. & Peebles, D.M, 2010; Cady, E. B, 1990; Roth, S. C., Baudin, J., Cady, E, 1997; Hanrahan, D., Cox, I. J., Azzopardi, D, 1999; Palmer, C., Brucklacher, R. M., Christensen, M. A, 1990)

This makes us think a hypothesis, the hypoxic-ischemic injury occurs in at least two phases: a primary defect on the brain energy production during the hypoxic-isquemic process that induces subsequent events; based on studies on global hypoxia-ischemia in newborns and focal cerebrovascular accident on baby rats. (Hanrahan, D., Cox, I. J., Azzopardi, D, 1999; Palmer, C., Brucklacher, R. M., Christensen, M. A, 1990)

Hypoxia in murines can be reflected on behavioral characteristics, such as correction and geotactic reflex, besides modifications on the righting reflex test (put rats on their back and record the time they take to set in prono with their paws on the floor). The objective of this investigation was to identify the main characteristics of the murines after been submitted to hypoxia.

Materials and Methods

An experimental study will be carried out, Wistar rats were submitted to hypoxia with an age of 0-10 days old, male, phenotypically normal, with a sample size of 11 rats, calculated and non-probabilistically chosen by convenience inside the assigned vivarium for this investigation.

The rats were evaluated before the hypoxic stimulus and after it, the rats were evaluated via geotactic reflex test, in which the rats were placed in a 45° iron pending (grating), of 30 cm in length, they were placed upside down in the center of the grid, the time rats took to turn around and face the upward slope was registered (torsion angle >90°.

The second test was the walk test through the grid. The rats walked through a wire mesh grid (3x3 cm, total area 29x29) for 2 minutes. A fail was counted when all the paw broke through the grid. The tests scores were calculated for the front and rear limbs as the proportion of failure of total steps.

Results

A total of 11 murines were obtained for this study, which were evaluated prior to hypoxic injury, recording 100% of normal functions in the assessment of the neuronal function, musculoskeletal strength, walk and righting reflex. The murines initial age was 14.5 (SD±1.51) days, their weight was 32.27 (SD±5.93) grams, with an initial age of 8 days in 100% of the cases.

After hypoxic stimulus, the neurogical function of all rats decreased, presenting lethargy in 81.8% of the cases, the neuromuscular strength remained without difficulty in 81.8%, with 18.2% with not valuable modification. The walk showed difficulties in 100% of the case, while the righting reflex showed an immediate recovery in 9.1% of the cases, with a reflex that is not recovered in 45.5% of cases and 45.5% with a late recovery. This can be seen in figures 1, 2, 3 and 4.

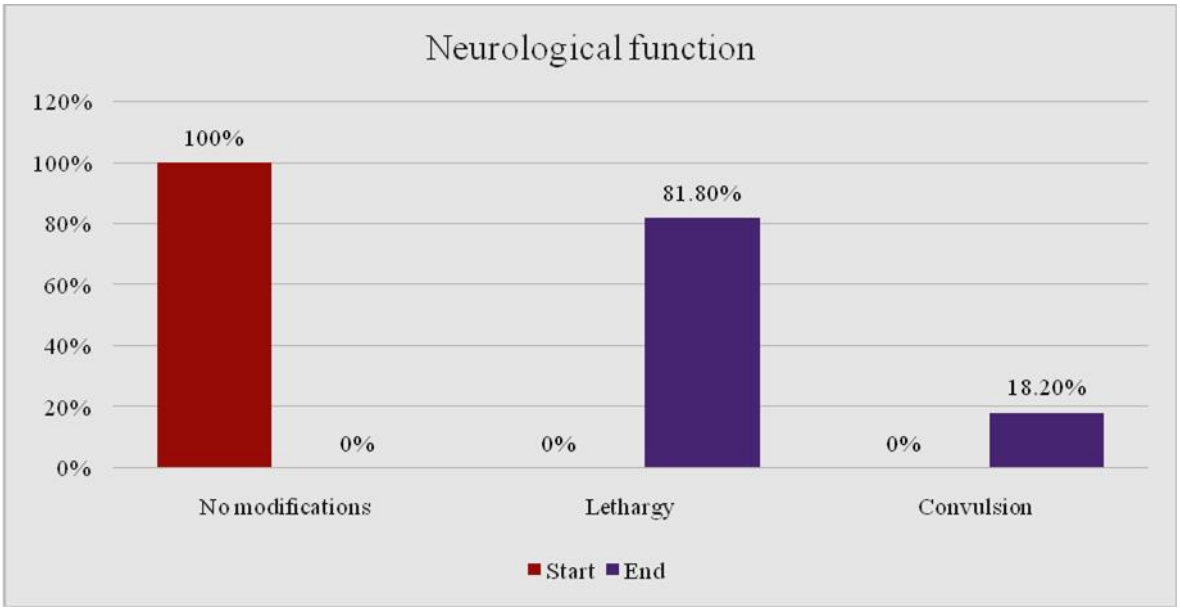

Figure 1. Assessment of neurological function after hypoxic stimulation

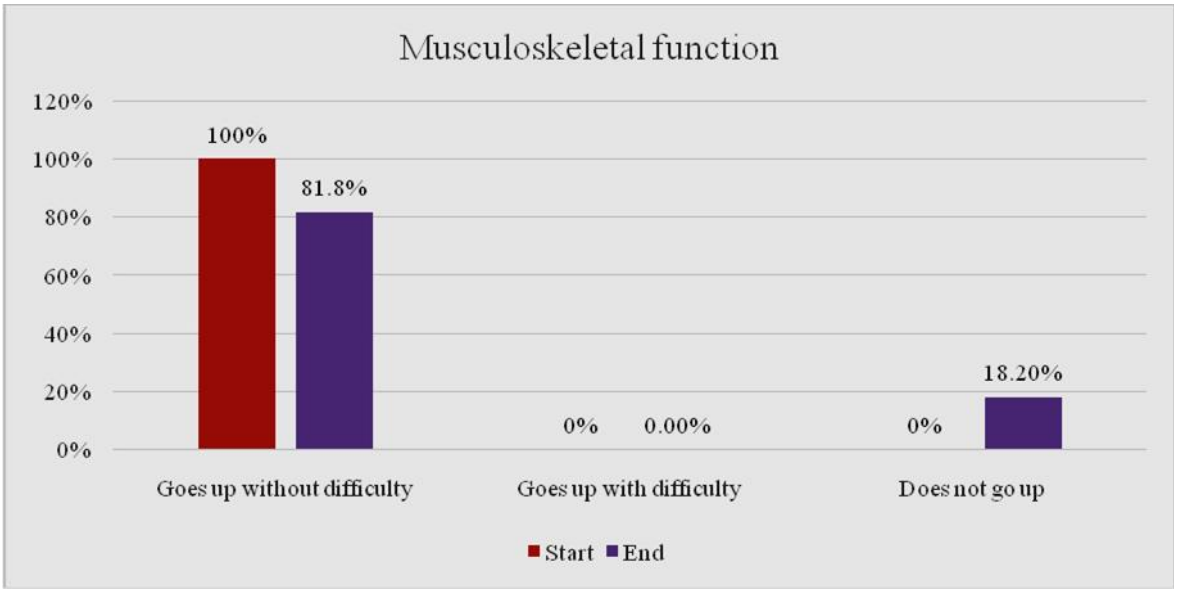

Figure 2. Assessment of musculoskeletal function after hypoxic stimulation

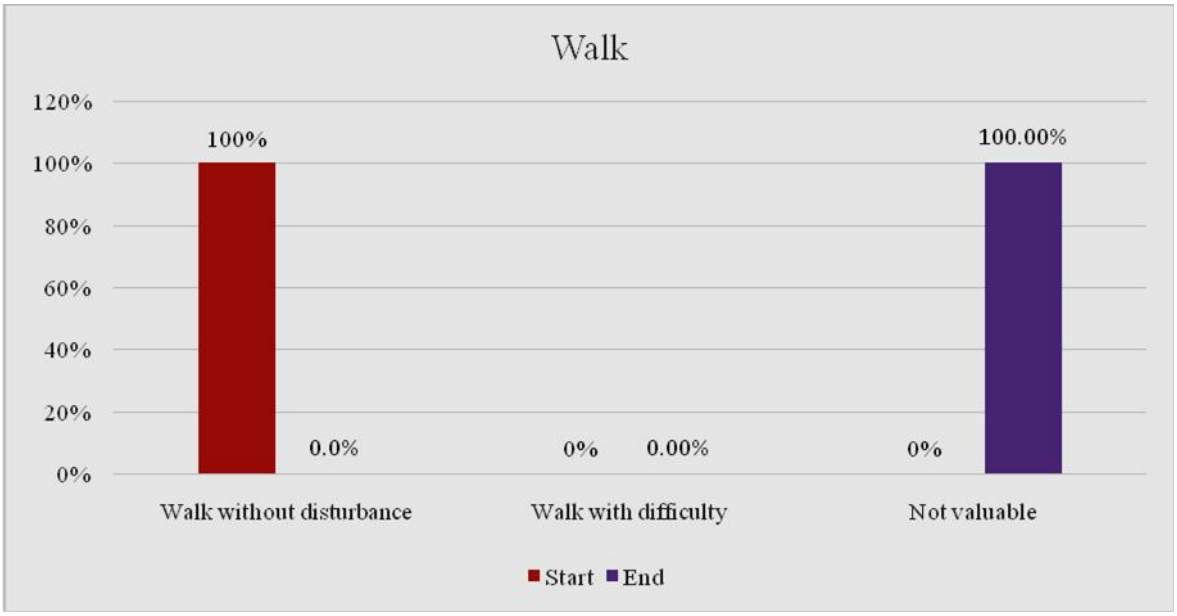

Figure 3. Assessment of walk after hypoxic stimulation

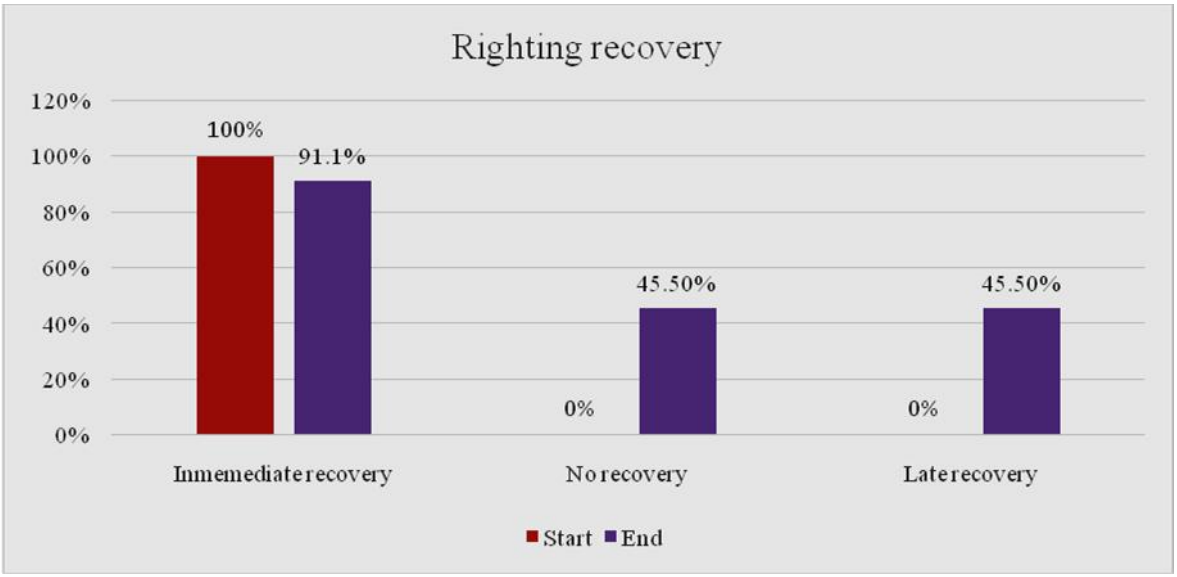

Figure 4. Assessment of righting recovery function after hypoxic stimulation

Discussion

As we can observe, hypoxia stimulus in murine neonates can be valued through different tests, however, musculoskeletal strength is the least affected, so, more evaluations are needed to determinate if it can be used as a parameter to evaluate the treated rats improvement to revert hypoxia consequences.

Nowadays, hyperbaric oxygen therapy (HBOT) has been successfully tested in many studies such as the treatment of cerebrovascular accident, brain trauma and neurological disease (Al-Waili, N. S., Butler, G. J., Beale, J., Abdullah, M. S., Hamilton, R. W. B., Lee, B. Y, 2005; Noori S. Al Waili, 2005; Rainer Kentner, Florence M. Rollwagen, 2002). This study mentions the experience of animals with ischemic injuries where early administration of HBOT reduces the size of cerebral global stroke and increases survival. Therefore, we consider pertinent to initiate studies focused on the hypoxia treatment in murine neonates, since there is a background that suggest early HBOT can improve the stroke area, and improving the neurological scores after 7 days of reperfusion with neuroprotective effects. (Al-Waili, N. S., Butler, G. J., Beale, J., Abdullah, M. S., Hamilton, R. W. B., Lee, B. Y, 2005; Noori S. Al Waili, 2005; Rainer Kentner, Florence M. Rollwagen, 2002)

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