



Research Article

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Implementation of an Effective Low-Cost Neonatal Hypothermia Program in Limited Resource Settings

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Abstract

Objectives: Neonatal therapeutic hypothermia decreases poor neurological outcomes, the implementation of an effective, low-cost Neonatal Therapeutic Hypothermia (NTH) Program in limited-resource settings where the incidence of perinatal asphyxia is high, is necessary. This program implementation objective is the improvement of Neurological outcomes in low resources settings following a high quality, evidence-based methodology for this treatment.

Methods: We describe Forty Asphyxiated Newborns enrolled from April 2013 to December 2014 with rectal temperature (RT) maintained at 32-34 °C with a new program based on a strict methodology according to clinical trials and emphatic care of specific points. NTH initiated after obtaining signed informed consent. Bayley Scales of Infant Development II (BSID-II) Psychomotor and Mental Development Index was used to assess neurological development Between 6 and 18 months.

Results: Children reached hypothermia within 2.5 hours on average; RT was <33 °C. Neurological development: Evaluated in 31 patients between 6 and 18 months of age. The baseline Mental development index (MDI) was <70 in 16%, 70-84 in 68% and >85 in 16% of the patients. At the end of the study, the MDI was <70 in 6%, 70-84 in 23% and was >85 in 71% of the patients. The baseline psychomotor development index (PMDI) was < 70 in 19%, 70-84 in 71% and >85 in 10%. After 6 months, the PMDI was <70 in 10%, 70-84 in 35% and >85 in 55%.

Conclusion: These data support the effectively of this quality improvement project for implementation of NTH in resource-limited settings.

Keywords: Neonatal therapeutic hypothermia; Neurological sequelae; Perinatal asphyxia

Abbreviations: NTH: Neonatal Therapeutic Hypothermia; RT: Rectal temperature; BSID-II: Bayley Scales of Infant Development II, MDI: The mental development Index; PMDI: Psychomotor Development Index; HIE: Hypoxic-Ischemic Encephalopathy; RR: Relative Risk; CI: Confidence Interval; MRI: Magnetic Resonance Image; HYLOCAN: Hypothermia Low Cost for Asphyxiated Newborns; AAP: American Academy of Pediatrics; AHA: American Heart Academy

Objective

Neonatal therapeutic hypothermia (NTH) is an approved treatment used in many parts of the world for reducing morbidity, mortality and disability in asphyxiated infants [1-3]. However, its use in low-income countries is limited, and the attempts to reduce its costs have not achieved optimal results [4-6]. Neonatal asphyxia-related deaths can decrease if the management is accessible to those who need it. The hypothermia decreases mortality and severe sequelae at 18 months of age is (relative risk (RR), 0.75;

95% confidence interval (CI), 0.68 to 0.83 [2]. Several studies support the beneficial effects of NTH such as a decrease in severe neuro developmental disability and mortality [1-3]. Comparative studies of total body hypothermia and selective head hypothermia revealed greater suppression of the release of free radicals [7] as well as lower-grade lesions in Magnetic Resonance Image (MRI) studies [8] in the case of whole-body hypothermia. In low-income countries the incidence of perinatal asphyxia is greater, neonatal

transport systems are slow, and there is significant geographic dispersion with poor roads, all of which make it difficult to provide hypothermia in a timely fashion. It is necessary to develop a system to produce stable cooling directly at the birthplace to reach more asphyxiated patients. The program's name is Hypothermia low Cost for Asphyxiated Newborns (HYLOCAN). American Academy of Pediatrics (AAP) and American Heart Association (AHA), 2015 Guidelines for Neonatal Resuscitation, recommend therapeutic hypothermia in resource-limited settings [9], we describe a whole-body hypothermia method similar to those used in published clinical trials, clearly defined and based on internationally accepted criteria.

Methods

The program was approved by the Human Research Ethics Committee of the Hospital and implemented for 21 months in the "Ajusco Medio" General Hospital, a second-level general public hospital located in an underserved area of the City of Mexico, which serves a low socioeconomic status population with little attachment to prenatal control programs. At this hospital, patients with HIE are treated following international protocols [1,3,10]. We included children who had completed 36 weeks of gestation, weight greater than 1800 grams with clinical data of asphyxia, diagnosed by one or more of the following: Apgar less than 5 at 10 minutes, assisted ventilation for more than 10 minutes, clinical seizures, pH less than 7.00 or base deficit greater than 16 in cord blood or pH less than 7.16 or base deficit greater than 10 the first hour of life with other indicators, and clinical evaluation with HIE moderate or severe according to Sarnat Criteria [11]. Exclusion criteria were as follows: the possibility of surgical intervention within 72 hours, major congenital malformation, multiple organ failures refractory to treatment, and parental rejection. Hypothermia was started within the first 6 hours of life, after obtaining signed informed consent, temperature range was established between 32–34 °C and was maintained for 72 hours, this is a manual device and in the beginning we use a broad range with the intention of facilitating the learning of the team, after ten patients we close the range to 32.5-33.5 °C. For cooling the newborn we used a disposable device, the COLD RUSH®-232000010 Model B, which is used to reduce post-arthroscopy inflammation in adults. It is a type of Cold Therapy System in which ice water is sent through hoses into a waterproof mat that is placed under a cotton sheet where the baby rests; this device has two-speed water circulation and maintains uniform cold diffusion. The main difference compared to other devices (Cool Cap® or Blanketrol®) is that regulation is manual and not servo-controlled. We used a water circulation sheet (Cincinnati Zero® SUB-874) that is compatible with the Cold Therapy System. The rectal temperature, heart rate, and blood pressure were registered hourly. The temperature was maintained stably in the desired range by increasing or decreasing the speed of the cooling device and regulation of radiant heat. When the treatment was completed, heating was performed by slowly increasing the temperature at a rate of 0.3-0.5 °C per

hour to reach 37 °C. Development was evaluated using the Bayley Scales of Infant Development II (BSID-II) Psychomotor and Mental Development Index each month. Thirty-one infants who had completed six months of age were included in the report. The average score of developmental assessments and the score from the last evaluation for both the Mental Development Index (MDI) and Psychomotor Development Index (PMDI) was considered. We made statistical analyses using the mean, range, Pearson chi-square and the joint likelihood comparative analysis. The joint likelihood method compares all the possible combinations, of the parameters of the model, from which the data could come from and gives a measure to compare them. The highest level of the joint likelihood method is 100%, and it is reached in the maximum likelihood estimator. Many different combinations of parameters would be as likely to produce the same observed data; This idea is captured by the contours. They show three things; every pair of values that are on the same contour are equally likely, every pair of values inside the contours would be more likely, and finally the values outside a given contour would be less likely to produce the data. Finally, if a pair of values is, for example, on the (1/10) x100 likelihood contour it means that the maximum likelihood estimator is ten times more likely to be the one that produced the data.

The project was implemented using the following process:

Step 1: Talk with all staff involved about the following educational objectives:

- a. Pathophysiology of asphyxia
- b. Physiology of hypothermia
- c. The utility of hypothermia
- d. Criteria for the application of hypothermia
- d. The method of application of hypothermia

Step 2: Development of resources for application in clinical areas

Laminated card A: Lists clinical criteria (placed in the cradle of resuscitation)

Laminated card B: Lists stabilization criteria pre-hypothermia (placed in the medical board area)

Concentration data sheet-Lists the parameters to be monitored each hour: temperature, heart rate and blood pressure, urinary volume. (placed on clinical records of each child)

Step 3: Daily monitoring of compliance with the criteria and analysis of the development of the child with hypothermia, by the Head of Service

Step 4: Evaluation of each case during and at the conclusion of the proceedings with all the doctors and nurses involved (debriefing).

Results

Table 1: Sample characteristics in 40 children undergoing hypothermia.

Gestational age (weeks)	39.4
ds(+/-)/range)	(+/-1.29) /37-42
Weight (grams)	2,965
ds(+/-)/range)	(+/-375)/2,240-4,030
Female (%) / male (%)	21(52%) / 19(48%)
Cesarean (%) / vaginal delivery (%)	14(36%) / 26(64%)
pH at birth (average/D.S.)	6.82 (+/-0.087)
pH < 7.0 (n/%)	27/67%
pH between 7.0-7.10 (n/%)	9/23%
pH > 7.11 (n/%) (with others inclusion criteria present)	4/10%
base deficit > 16 (n/%)	30/75%
> 10 minutes Assisted ventilation at birth	18/45%

Table 2: Temperature characteristics.

Hours after birth to reach hypothermia (mean / sd)	2.52(+/- 1.94)
hours hypothermic (mean / sd)	73.2 (+/-2.08)
Measurements outside range n / total measurements (%)	48/2931 (1.63%)
first 10 patients	25/728 (3.47%)
second 10 patients	9/736 (1.25%)
third 6 patients	7/731 (0.95%)
last 10 patients	7/734 (0.95)
determinations out of range < 32 °C	37/42 (76%)
determinations out of range > 34 °C	11/42 (24%)

40 babies with mod-severe HIE cooled over 20 months. The population characteristics are shown in (Table 1). The method was possible in all the patients and technically we don't found a problem with the implementation, Temperature control to the target rectal temperature was in desired range by 98.4% and improved with experience showing difference between the first 10 patients and the last 10 patients (Table 2) the learning curve was easily dominated. 12.5% of the patients received platelet transfusions, and 15% had seizures during hypothermia. Neurological development was evaluated in 31 patients who had completed between 6 and 18 months of age. After six months both development index improved, the mental development index (MDI) was >85 in 71% and psychomotor development index (PMDI) was >85 in 55% (Table 3). We use a Pearson's Chi-Square Test to prove the null hypothesis that HYLOCAN method is equivalent to Azzopardi's method, and the result is that we can reject the null hypothesis in both cases, mental development (with p-value 0.016) and motor development (with p-value 0.0024). Finally, the contours for the joint relative likelihood show that for a level of 5% of the likelihood the method is effective using Azzopardi work as a reference as it is presented in (Figure 1). As

it was done for the mental development, the contours for the joint relative likelihood shows that for a level of 20% of likelihood is our method is effective using Azzopardi work as a reference as it is presented as it is shown in (Figure 2).

Table 3: Results of neurodevelopmental tests in the initial evaluation and at 6 -18 months measured by Bayley Scales of Infant Development II (BSID-II) Psychomotor and Mental Development Index.

	Initial Mental Index Average	6-18 months Mental Index	Initial Motor Index Average	6-18 months Motor Index
<70	5/31(16%)	2/31(6%)	6/31(19%)	3/31(10%)
70-84	21/31(68%)	7/31(23%)	22/31(71%)	11/31(35%)
>85	5/31(16%)	22/31(71%)	3/31(10%)	17/31(55%)

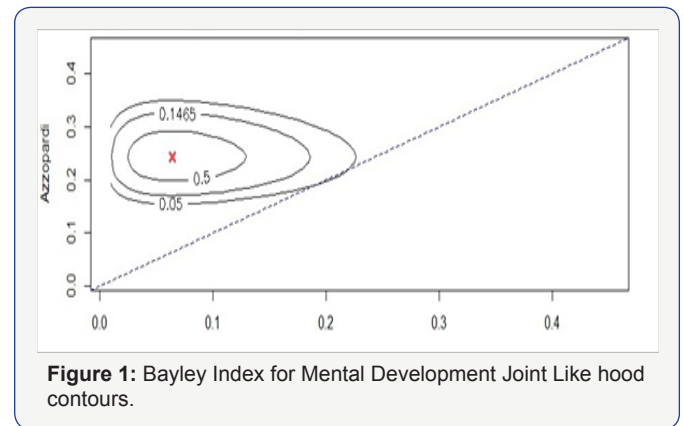


Figure 1: Bayley Index for Mental Development Joint Likelihood contours.

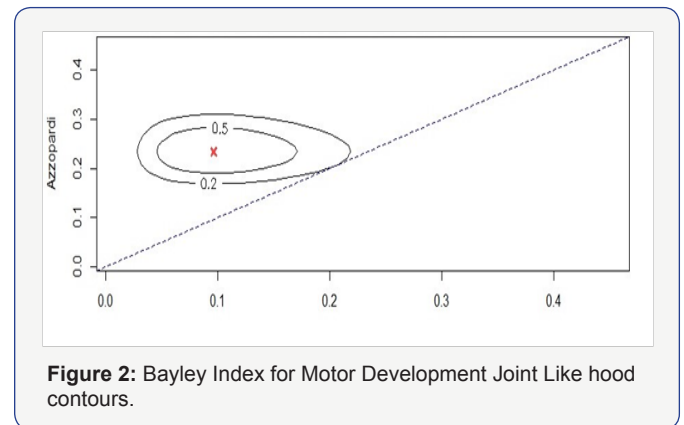


Figure 2: Bayley Index for Motor Development Joint Likelihood contours.

Discussion

The implementation of the program was friendly and was accepted by staff and parents, the neonatologist team was more doubts, and used more frequently amines and more invasive approach, the pediatric team followed the method more closely and had fewer problems. The technical implementation revealed that temperature management and the detection and management of complications is possible and easy with intensive care of critical specific points. Neurodevelopment outcomes are positive with an initial evaluation of little damage, and patients showed excellent responses to neurodevelopment treatment: the

final number of children with severe squal below 70 was similar to the results published by Azzopardi et al. [12]. (Table 4) In our study, for ethical reasons, we did not establish a control group without hypothermia. Our study reveals that HYLOCAN is an effective and safe program to provide hypothermia in the neonatal intensive care unit (NICU) of a second-level General Hospital where nearly 1% of children are born with neonatal asphyxia. The HYLOCAN program (Hypothermia Low Cost for Asphyxiated Newborns) is a model applicable to low-income units and allows providing hypothermia during the first hours of life. We believe that the systematic training of personnel, continuous monitoring and feedback processes (debriefing) can quickly overcome the learning curve and provide a safe, efficient and cheaper method for hypothermia. In many hospitals, therapeutic hypothermia for perinatal asphyxia is not routinely administered, probably due to lack of staff training and the cost of treatment. The work of Jacobs et al. shows the possibility of use Hypothermia in a hospital with resource limitations [13], Devices for servo-controlled hypothermia cost thousands of dollars and use expensive disposable accessories; these devices cost much more than the disposable device used in our studies (230 USD). We must also take into account the cost of supplies required for each patient treated with NTH, which is lower in our study (10 USD). Previous reports show effective achieving of desired temperature using active control, archives target temperature in an easy way and maintains the stability [14]. In many parts of the world, there are hospitals with limited resources, where the potential neonatal candidates for hypothermia can reach 2.7 per 100 births, the exact number is unknown; however, if we assume that 60% of the population is similar in demographic characteristics to the people of this study the number of asphyxiated patients potentially benefited is very large. The use of this program has the potential to decrease the incidence of neurological sequelae and allowing to a lot of these children to develop normally.

Table 4: Outcome at 18 months compared with Azzopardi.

	HYLOCAN	Azzopardi [9]
Death	0/23 0%	42/163 -26%
IndexBayley Mental Development	6 -18 months	18 months
<70	2/31-6%	28/115 -24%
70-84	7/31 -23%	6/115-5%
>85	22/31 -71%	81/115 -70%
IndexBayley Motor Development	6 -18 months	18 months
<70	3/31(10%)	27/114 (24%)
70-84	11/31(35%)	9/114 (8%)
>85	17/31(55%)	78/114 (68%)

We believe that any method that provides therapeutic hypothermia on a large scale in low-income countries should fulfill the following criteria:

1. Affordability.
2. Ability to provide hypothermia with minimal patient transfers.
3. A simple and easy scheme for the staff involved.
4. Close monitoring of compliance with goals and objectives.
5. Patience, analysis, and feedback to master the learning curve.

Conclusion

This study demonstrates the feasibility of efficient and safe low-cost methods of cooling in a second level hospital with positive neurodevelopment outcome compared with international studies. It could be used in low resources environments throughout the world. Depriving an asphyxiated child of the opportunity to undergo treatment with hypothermia is a significant therapeutic failure and implementation of this treatment in low-resource settings is a medical priority. Based on our analysis, the HYLOCAN program can be developed as an important tool for hypothermic treatment in places with limited resources.

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Contributors' Statements

Claudia Calderon-Jimenez: Dr. Calderon designed the study, controlled the clinical application, drafted the initial manuscript, and approved the final manuscript as submitted.

Rolando Rivera-Gonzalez: Dr. Gonzalez carried out the initial analyses, make the neurological evaluation, reviewed and revised the manuscript, and approved the final manuscript.

José Nuñez-del-Prado: Dr. Nuñez-del-Prado made the final analyses, critically reviewed and revised the manuscript, and approved the final manuscript.

Pedro Orozco Del Pino: Mr. Orozco Del Pino designed the data collection instruments, and coordinated and supervised data, critically reviewed the manuscript, and approved the final manuscript as submitted.

Alberto Orozco-Gutierrez: Dr. Orozco Gutierrez conceptualized and designed the study, drafted the initial manuscript, made the final analyses, reviewed, revised and approved the manuscript,

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

References

1. Shankaran S, Laptook AR, Ehrenkranz RA, Tyson JE, McDonald SA, et al. (2005) Whole-body hypothermia for neonates with hypoxic-ischemic encephalopathy. *N Engl J Med* 353(15): 1574-1584.
2. Jacobs SE, Berg M, Hunt R, Tarnow-Mordi WO, Inder TE, et al. (2013) Cooling for newborns with hypoxic ischaemic encephalopathy. *Cochrane Database Syst*.
3. Garfinkle J, Sant'Anna GM, Wintermark P, Ali N, Morneault L, et al. (2013) Cooling in the real world: therapeutic hypothermia in hypoxic-ischemic encephalopathy. *Eur J Paediatr Neurol* 17(5): 492-497.
4. Pauliah SS, Shankaran S, Wade A, Cady EB, Thayyil S. (2013) Therapeutic hypothermia for neonatal encephalopathy in low- and middle-income countries: a systematic review and meta-analysis. *PLoS One* 8(3): e58834.
5. Kim JJ, Buchbinder N, Ammanuel S, Kim R, Moore E, et al. (2013) Cost-effective therapeutic hypothermia treatment device for hypoxic ischemic encephalopathy. *Med Devices (Auckl)* 6: 1-10.
6. Laptook AR (2009) Use of therapeutic hypothermia for term infants with hypoxic-ischemic encephalopathy. *Pediatr Clin North Am* 56(3): 601-616.
7. Ikeda K, Ikeda T, Taniuchi H, Suda S (2012) Comparison of whole-body cooling and selective head cooling on changes in urinary 8-hydroxy-2-deoxyguanosine levels in patients with global brain ischemia undergoing mild hypothermia therapy. *Med Sci Monit* 18(7): CR409-414.
8. Sarkar S, Donn SM, Bapuraj JR, Bhagat I, Barks JD (2012) Distribution and severity of hypoxic-ischaemic lesions on brain MRI following therapeutic cooling: selective head versus whole body cooling. *Arch Dis Child Fetal Neonatal Ed* 97(5): F335-339.
9. Wyckoff MH, Aziz K, Escobedo MB, Kapadia VS, Kattwinkel J, et al. (2015) Neonatal Resuscitation: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care *Circulation*. 132: S543-S560.
10. Buonocore G, Perrone S, Turrisi G, Kramer BW, Balduini W (2012) New pharmacological approaches in infants with hypoxic-ischemic encephalopathy. *Curr Pharm Des* 18(21): 3086-3100.
11. Sarnat HB, Sarnat MS (1976) Neonatal encephalopathy following foetal distress: a clinical and electroencephalographic study. *Arch Neurol* 33(10): 696-705.
12. Azzopardi DW, Strohm B, Edwards AD, Dyet L, Halliday HL, et al. (2009) For the TOBY Study Group. Moderate Hypothermia to Treat Perinatal Asphyxial Encephalopathy. *N Engl J Med* 361(14): 1349-1358.
13. Jacobs SE, Morley CJ, Inder TE, Stewart MJ, Smith KR, et al. (2011) Infant Cooling Evaluation Collaboration. Whole-body hypothermia for term and near-term newborns with hypoxic-ischemic encephalopathy: a randomized controlled trial. *Arch Pediatr Adolesc Med* 165(8): 692-700.
14. Goel N, Mohinuddin SM, Ratnavel N, Kempley S, Sinha A (2017) Comparison of Passive and Servo-Controlled Active Cooling for Infants with Hypoxic-Ischemic Encephalopathy during Neonatal Transfers. *Amer J Perinatol* 34(1): 19-25.



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