Treatment Device for Neonatal Birth Asphyxia Related Hypoxic Ischemic Encephalopathy

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Abstract

Background: Birth asphyxia is a leading cause of neonatal brain injury, morbidity and mortality globally. Birth asphyxia leads to multi-organ dysfunction in the neonate and to neurological dysfunction called Hypoxic Ischemic Encephalopathy (HIE). Cooling therapy is being used as a means of treatment in developed countries. However, these devices are not affordable for low-resource settings, including Ethiopia. Moreover, many cooling devices do not have a rewarming functionality after cooling therapy. The objective of this project was therefore to design and develop a cost effective and efficient total body cooling and rewarming device.

Methods: Our design includes two water reservoirs that operate by pumping cold and warm sterile water to a mattress. After decreasing the core body temperature of the infant to 33.5 °C, the system is designed to maintain this temperature value for 72 hours. Feedback for temperature regulation will is provided by rectal temperature sensor. Once the cooling therapy is completed, the system again rewarms the water inside the matters and gradually increases the neonate temperature to 36.5-37 °C. The device also allows continuous monitoring of infant’s body temperature, mattress temperature reservoir temperature and pulse rate.

Results: The prototype was built and undergone through different tests and iterations. The proposed device was tested for accuracy, cost effectiveness and ease to use. 93.2 % accuracy has been achieved for temperature sensor measurement and the prototype was built only with a component cost of less than 200 USD.

Conclusion: The proposed devices allow an accurate, regulated and continuous monitoring of temperature of reservoirs, mattress and rectal temperature. was provided using sensors. The device can play a significant role by reducing neonatal brain injury and death due to HIE, especially in low resource settings, where the expertise and the means are in scarce.

1. Background

Birth asphyxia is a medical condition that causes deprivation of oxygen to a newborn infant before and during birth. Hypoxic-ischemic encephalopathy (HIE) is a brain injury caused by impeded flow of oxygenated blood to a baby’s brain around the time of birth. It is the leading cause of neonatal brain injury, morbidity, and mortality globally (1). Perinatal asphyxia may affect virtually any organ, but HIE is the most studied clinical condition and that is burdened with the most severe sequelae (2). When an infant is affected with HIE, a neuron damage will occur and that neuron damage generates free radicals. It occurs in 50–60 % of babies with perinatal asphyxia (3). The degree of neonatal encephalopathy at birth can be categorized into three stages; stage 1, 2 and 3 (4, 5). Infants who experience moderate HIE have a 10% risk of fatality, and those who live have a 30% risk of disabilities (6). Infants with severe HIE have a 60% risk of fatality, and nearly all of the survivor’s experience disabilities (5).
Literature shows that birth asphyxia is a universal public health problem with varied significance country wise. Worldwide, 23% of neonatal deaths and 10% of all deaths in children under 5 years of age are estimated to occur because of birth asphyxia (7–10). In sub-Saharan Africa infant deaths account for 38% of global neonatal mortality due to preventable causes including perinatal asphyxia (11).

A careful neurologic examination needs to be performed to diagnose HIE. History of prolonged and difficult labor coupled with need for significant resuscitation, low Apgar scores, altered sensorium and early onset seizures usually point towards HIE. There is increased risk of neonatal encephalopathy if the mother has fever during antepartum or intra-partum period (12). Imaging modalities including Magnetic Resonance Imaging (MRI), Computerized Tomography (CT), and Ultrasound (US) are also used to diagnose HIE. MRI is the most sensitive imaging modality for detecting hypoxic brain injury in the neonate (13). CT scans may be helpful to determine focal hemorrhagic lesions or large arterial ischemic strokes. US can be useful for excluding hemorrhagic lesions despite its limited utility in evaluation of hypoxic injury in the term infant (14). Accurate diagnosis of HIE leads to early and effective treatment.

Body cooling has been proposed as an effective treatment for HIE in many animal and human experiments (15–19) Experiment on animal was conducted by Jacek et. Al (19) on selective brain hypothermia, which is applied via a cranial window after decompressive craniotomy and a reduction in posttraumatic structural and functional damage has been observed. However, the study was actually limited by small rodent model and short observational period. Horn et. Al (18). used a servo-controlled fan device to cool 10 infants with neonatal encephalopathy. Infants were nursed on a servo-controlled radiant warmer, set to a target of 33.4°C-33.7°C. However, shivering in half of the cases with higher fan speeds and a generally undeniable degree of nursing monitoring compared to servo-controlled systems was noticed. Moreover, the proposed method requires a substantial amount of equipment making it complex and expensive for low resource settings.

In general, body cooling treatment devices are frequently used to treat neonates with HIE in many developed countries. Cooling equipment used in developed countries are costly, requires maintenance and has recurring costs. Many cheap cooling techniques are labor intensive and may result in temperature fluctuations as well as shivering with a potential loss of neuro-protective efficacy (20). Moreover, a separate rewarming device, usually radiant warmers are used to rewarm the infant after the cooling therapy, causing additional burden to the healthcare system and infant families. This is especially a challenge in many developing countries, where the resources are in scarce. In this paper a safe, cost effective and efficient dual whole-body cooling and rewarming device is proposed for neonatal birth asphyxia related HIE.

2. Method

2.1. The Proposed design
In this study, we proposed a dual whole-body cooling and rewarming device for neonatal birth asphyxia related HIE. This automatic cooling and warming device have two reservoirs one for cooling and another for warming purpose. The proposed design solution includes temperature sensors, hot and cold-water reservoirs, Arduino Mega controller, Solenoid valves for hot and cold water, Peltier cooling and warming device, relays, water pump, mattress, buzzer and LCD display.

This auto-regulated cooling and heating method uses a thermoelectric cooler which is known as Peltier device to cool and heat two water reservoirs. The Peltier inside the reservoirs can cool the water as well as work in reverse mode and produce heat in order to warm the sterile water. The system works by automatically controlling the rotation of the cold and warm water to the specially designed infant mattress based on the value from the rectal and mattress temperature sensor values. Figure 1 demonstrates the functional block diagram of the proposed method.

The preparatory phase of the system begins by filling water to the reservoirs till their full capacity. When the power is turned ON, the system powers up the cooling system in reservoir-one and at the same time it powers up the heating system in reservoir-two. Simultaneously the temperature sensors in both reservoirs will be initiated. Then the user will be prompted to select the temperature values to which the water is to be cooled and warmed. The set point of temperatures may vary depending on the environment air condition in which the treatment is being given (12 °C – 17 °C for cooling and 37 °C – 39 °C). When the coolant reaches the set temperature value, water will be pumped into the neonate mattress.

In cooling phase, the rectal temperature sensor and mattress water temperature sensor values will be used to monitor the system. When the temperature of water in the neonate’s mattress increases and the temperature of neonate is above 33.5 °C, a cold water will be pumped in from reservoir-one and warm water will leave the neonate’s mattress. Until the required temperature is achieved, the cold and warm water will be rotated in controlled fashion. This flow of water is controlled by the integration of the DC motor pump and the solenoid valves. The main target of this rotation is to sustain the neonate body temperature at 33.5 °C for 72 hours, which is called therapy phase.

An alarm will be activated if the rectal temperature is less than 32.5 °C or greater than 34.5 °C during the therapy phase. After 72 hours of therapy phase, the rewarming phase begins. The earlier cold water in the neonate mattress will be replaced by the warm water. Up on completion of the hypothermia period, a 6 to 10-hour rewarming process begins during which the baby is warmed at gradual rate of 0.5 °C per hour or less until it reaches a core temperature of 36.5 °C and stabilizes. If the rectal temperature increases more than 0.5 °C/hour, the alarm will be initiated. The therapy will be completed if the rectal temperature reaches 36.5–37 °C. The sensors result including set temperature, water temperature in cold and hot reservoir, rectal and skin temperature and mattress temperature are continuously displayed on LCD.

### 2.2. Temperature regulation phases

The proposed system is design to control regulate temperature for three phases: preparatory phase, cooling phase, therapy phase and rewarming phase.
2.2.1. The preparatory Phase

The preparatory phase begins by filling water to the reservoirs until their capacity. In this phase, the coolant will be made ready to be applied to the neonate for therapy. The steps in the preparatory phase include:

- Turning the device ON – powers up the system.
- When power is turned ON Arduino powers up the temperature sensors in the cold reservoir and hot reservoir.
- The temperature detected by the temperature sensor is displayed on the LCD, “current temperature of cold liquid”. current temperature of hot liquid”.
- Then the system prompts the user to “Enter” the temperatures to which the water is to be cooled and warmed (desired temperature of coolant and desired temperature of warmer).
- The cooling and warming system will be initiated to operate until the set points are reached in the reservoirs.
- When the temperature of coolant reaches the set point, the microcontroller commands the cooling system to stop cooling, powers up the DC motor pump and solenoid valve 1 through a relay simultaneously.
- Normally closed solenoid valve 1 now becomes open for the flow of coolant liquid into the neonate mattress.
- After the mattress is filled, the microcontroller sends a command to turn OFF the DC motor pump and solenoid valve 1.
- Rectal temperature sensor is firmly attached to the rectum of the neonate.

2.2.2. The Cooling Phase

The steps of the cooling phase include:

- The jack of rectal temperature sensor connects to the device.
- The microcontroller powers up the rectal temperature sensor.
- A text “Cooling Phase” displayed on the LCD.
- Neonate’s rectal temperature will be displayed on the LCD.
- The detected rectal temperature will be displayed on the LCD, “rectal temp.”
- A text “cooling is initiated” will be displayed on the LCD.
- When temperature of neonate is above 33.5, the water from the cold reservoir will be pumped in to the mattress. So, the microcontroller powers up the relay to turn ON the DC motor pump and the solenoid valve 1 while simultaneously opening solenoid valve 2 to let go the existing mattress water.

2.2.3. The Therapy Phase
Steps in therapy phase include:

- when the rectal temperature became $33^\circ C$ the microcontroller activates solenoid valve 2 and DC motor pump to let the warm water to enter into the neonate's mattress.
- If the rectal temperature is less than $32.5^\circ C$ during therapy phase, the microcontroller will activate the buzzer and a text “Over Cooling” will be displayed on the LCD.
- The existing warm water will be removed from the neonate's mattress
- The process continues until a rectal temperature reaches $33.5^\circ C$ and a text “Therapy Phase” will be displayed on the LCD.
- If the rectal temperature is greater than $34.50^\circ C$ during therapy phase, the microcontroller will activate the buzzer and a text “Over Heating” will be displayed on the LCD.
- The existing warm water will be then removed from the neonate's mattress
- The process continues until a rectal temperature reaches $33.5^\circ C$.

### 2.2.4. The Rewarming Phase

The following are the steps of the rewarming phase.

- After 72 hours of therapy phase, the microcontroller will activate the DC motor pump and solenoid valves simultaneously.
- A text “Warming Phase” will be displayed on the LCD.
- The existing cold water in the neonate mattress will be replaced by the warm water
- When the mattress fully filled, the microcontroller will command the DC motor pump and the solenoid valve to be turned off.
- If the rectal temperature increases more than $0.5^\circ C/hr$, the alarm will be activated
- When the rectal temperature reaches $37^\circ C$, a text “Therapy Completed” will be displayed on the LCD.

### 2.3. Materials Used

Table 1 demonstrates the materials used to construct the prototype.
Table 1
List of materials and specification used to construct the prototype

| S. No | Items                | Specification  |
|-------|----------------------|----------------|
| 1     | Peltier              | 12V DC         |
| 2     | Fan                  | 12V DC         |
| 3     | Arduino              | Arduino Mega   |
| 4     | DC motor             | 12 V           |
| 5     | Solenoid valve       | 12 V           |
| 6     | Mattress             | Plastic        |
| 7     | Power supply         | 12 V           |
| 8     | Water temperature sensor | DS18B20    |
| 9     | Skin temperature sensors | LM35       |
| 10    | LCD                  | 16x2           |
| 11    | Reservoir type       | Plastic        |
| 12    | Relay                | 12v            |
| 13    | Buzzer               | Buzzer         |
| 14    | LED                  | 16x2           |
| 15    | Keypad               | 4x4            |
| 16    | Heat sink            | Al heat sink   |
| 17    | Tubes                | PVC            |

3. Results

3.1. Simulation Result

The design was simulated using Proetus Simulation software and Arduino IDE prior to prototype construction. The inputs used for the simulated system were cold water temperature value from reservoir-1, warm water temperature value from reservoir-2, rectal and skin temperature values and treatment time. The system works by accepting input from the sensors. Based on the rectal and skin temperature input, water circulates between the reservoirs and mattress. Rectal and skin temperature, cold and warm reservoir temperatures, and heart rate and mattress temperature values are displayed on the LCD. An alarm was activated when the temperatures are above the target set values. Body and rectal sensors are continuously displayed on LCD. Figure 2 demonstrates the snapshoot of the proposed design simulation.
3.2. Prototype Iterations

Different prototype iterations have been conducted to modify our design. Figure 3 shows the hand sketched and the 3D design of the proposed device. Figure 4 shows the initial and final prototype. Initially, the body of prototype was constructed from waste materials. After initial prototype testing, the whole body of the device was constructed from wood.

3.3. Prototype Test Results

The design criteria used to design and construct the prototype were accuracy, safety, cost, portability and easy to use. The tests results were conducted against the design criteria. Accordingly, the accuracy of the prototypes units was checked by performing different tests. The accuracy of water temperature sensors in reservoir were tested by adding required amount of water (1000 ml) to the reservoir and cooling or warming it to the required level of temperature using Peltier. Then a digital thermometer was used as a gold standard to compare with the sensor’s readings. Following the same procedure, the accuracy of water temperature in the mattress was also tested. Table 2 demonstrates the testing methods and test results obtained.

| S.No. | Design criteria to be tested | Method | Result |
|-------|-----------------------------|--------|--------|
| 1     | Temperature measurement Accuracy | By measuring the Peltier temperature and mattress temperature sensor readings against digital thermometer | Accurate 93.2% |
| 2     | Electrical Safety | The system and mattress are isolated | Isolated system and emergency switch |
| 3     | Cost | Component cost | About 8000 Ethiopian Birr (ETB) |
| 4     | Portability | Weight measuring | 5 KG |
| 5     | Easy to use | Operating procedure | 30 min training for Physicians |

4. Discussion

Birth asphyxia, which is a medical condition resulting from deprivation of oxygen to a newborn infant before and during birth, is a common cause of mental retardation, cerebral palsy and other neurodevelopmental disorders. It causes neonatal encephalopathy and permanent severe neurologic impairment also known as Hypoxic-ischemic encephalopathy (HIE) HIE is a brain injury caused by
impeded flow of oxygenated blood to a baby’s brain around the time of birth. It is the leading cause of neonatal brain injury, morbidity, and mortality globally.

Although the infant health complexities due to HIE is extremely high in developing countries, Health facilities in low resource settings including Ethiopia have no access of proper HIE treatment device.

Neonatal therapeutic hypothermia is used to treat HIE by cooling the baby to about 33.5–34.5 oC degrees Celsius for 72 hours, ideally within six hours of birth/the oxygen-depriving event. Body cooling treatment devices are frequently used to treat neonates with HIE in many developed countries. However, a separate rewarming device, usually radiant warmers are used to rewarm the infant after the cooling therapy, causing additional burden to the healthcare system and infant families. Moreover, these cooling devices and warming devices are not available or limitedly available in developing countries.

In this paper we introduced a standalone autoregulated cooling and warming system for neonates with birth asphyxia related HIE. The device consists of temperature sensors, hot and cold-water reservoirs, Arduino Mega controller, solenoid valves for hot and cold water, Peltier cooling and warming device, relays, water pump, mattress, buzzer and LCD display. The sensors were used to detect the real-time temperature values from the mattress, skin and reservoirs. These values are then used by the controller to regulate the temperature of the water in the two reservoirs as required and the flow of water using solenoid valves, relays, DC motor pump and Peltier. The real-time temperature readings are continuously displayed in the LCD.

The proposed method was first simulated prior to prototype constructions. The body of the final design was constructed from locally available wood material. The design was simple and user friendly. This helps physicians to easily adapt the proposed system with a minimum training. The components of the prototype costs only 8000 ETB (approximately 160 USD) making it potentially affordable for low resource settings. The accuracy of the sensors used has been tested against a gold standard. An average accuracy of 93.2% was achieved for the temperature readings. Since the mattress and the main device are electrically isolated, the proposed design provides high level of safety.

5. Conclusion

In this paper a device that can accurately monitor and regulate the neonate core body temperature at the neuroprotective range is designed and developed. Two separate water reservoirs were, one for cooling and the other for rewarming were used. Since there is no cost effective and efficient treatment device for birth asphyxia related HIE in low- and middle-income countries, this device can fill the gap by providing safe, efficient and reliable way of treating treatment HIE with an affordable cost. The prototype was built and undergo through different tests and iterations and it the average accuracy of the temperature sensor readings was 93.2% accurate. The proposed method will have a great impact reducing neonates’ mortality in low resource settings where both the expertise and means are in scarce.
Declarations

1. Ethics approval and consent to participate

This research did not involve human, animals or other subjects. According to Jimma University’s institutional review board (IRB), no formal ethics approval was required in this particular case.

2. Accordance

This research has been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

3. Consent for publication

This research did not involve human, animals or other subjects

4. Competing interests

The authors declare that they have no competing interests

5. Funding

Not applicable

6. Authors’ contributions

GL and KD are the overall coordinators of this study, and they conceptualized, designed, and implemented in collaboration with the main investigators RZ, LG, GD, AO and GI. All authors contributed to the preliminary study, the design, prototyping and testing. The article was drafted by GL, taking into account the comments and suggestions of the coauthors. All coauthors had the opportunity to comment on the manuscript and approved the final version for publication.

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Figures
The block diagram of the proposed auto regulated cooling and heating device using two reservoirs (water bags).

Figure 2
Simulation of the autoregulated cooling and warming system. The proteus connection was done in wireless mode.
Figure 3

3D design of the proposed device using AutoCAD
Figure 4

The first and final prototype