EFFECTS OF WHOLE BODY COOLING AND MAGNESIUM SULFATE ON INFANTS WITH HYPOXIC-ISCHEMIC ENCEPHALOPATHY TREATMENT

Rania Reafaat Abdelkader Atia[1], Manal Mohamed Ahmed Ayed[2], and Saeedah H Aljadani[3]

[1] Physiology department Faculty of Medicine Zagazig University and Basic Medical Science Faculty of Applied Medical Science AlBaha University,Al-Baha,SaudiArabia, [2]Pediatric Nursing, Faculty of Nursing, Sohag University, [3] Department of Basic Sciences, Faculty of Applied Medical Sciences, Al-Baha University, Al-Baha, Saudi Arabia.

Corresponding author:
Manal Mohamed Ahmed Ayed

Mobile: +20 : 01021079610

e.mail:
manal_ayed@yahoo.com,
Received: 25/3/2023
Accepted:15/4/2023

Online ISSN: 2735-3540

ABSTRACT:

Background: *In neonates with moderate-to-severe hypoxia-ischemia encephalopathy (HIE), Therapeutic hypothermia (TH), which can be achieved by either whole-body or localized head cooling, lessens brain damage, offers neuroprotection, and lowers mortality rates, especially if initiated within the first six hours after birth. Moreover, adjuvant therapy like magnesium sulfate (MS) management offers increased neuroprotection. The goal of the interventional, randomized, controlled study was to evaluate the short-term effects of using TH alone or in conjunction for the treatment of newborn infants with MS as a neuroprotective medication with HIE.*

Aim*: to evaluate the effects of whole-body cooling and magnesium sulfate on infants with hypoxic-ischemic encephalopathy treatment.*

Patients and methods*: 39 newborns who met the HIE criteria and were born in the Neonatal Intensive Care Unit at Sohag University Hospital were enrolled in the study. They were split equally across the three groups; During the first six hours of life, Group 1 (n 13) received whole-body cooling as the only therapy; In addition to MS, Group 2 (n 13) received whole-body cooling as adjuvant therapy, while Group 3 (n 13) received supportive acute care interventions as a comparison.*

Results*: The TH plus MS group (group 2) had significantly better short-term outcomes when compared to other groups managed by TH (group 1) or supportive treatment, as indicated by a brief period of mechanical ventilation and respiratory support (p-value 0.001), a decrease in the incidence of convulsions (p-value 0.001), and an early start to feeding (p-value 0.001) (p-value 0.009) (group 3). Conclusion: In addition to MS, total body cooling is a safe therapy that enhances short-term clinical and radiological outcomes for the treatment of HIE infants.*

In neonates with moderate-to-severe hypoxia-ischemia encephalopathy (HIE), Therapeutic hypothermia (TH), which can be achieved by either whole-body or localized head cooling, lessens brain damage, offers neuroprotection, and lowers mortality rates, especially if initiated within the first six hours after birth. Moreover, adjuvant therapy like magnesium sulfate (MS) management offers increased neuroprotection. The goal of the interventional, randomized, controlled study was to evaluate the short-term effects of using TH alone or in conjunction for the treatment of newborn infants with MS as a neuroprotective medication with HIE. Aim: to evaluate the effects of whole-body cooling and magnesium sulfate on infants with hypoxic-

ischemic encephalopathy treatment. Patients and methods: 39 newborns who met the HIE criteria and were born in the Neonatal Intensive Care Unit at Sohag University Hospital were enrolled in the study. They were split equally across the three groups; During the first six hours of life, Group 1 (n 13) received whole-body cooling as the only therapy; In addition to MS, Group 2 (n 13) received whole-body cooling as adjuvant therapy, while Group 3 (n 13) received supportive acute care interventions as a comparison. Results: The TH plus MS group (group 2) had significantly better short-term outcomes when compared to other groups managed by TH (group 1) or supportive treatment, as indicated by a brief period of mechanical ventilation and respiratory support (p-value 0.001), a decrease in the incidence of convulsions (p-value 0.001), and an early start to feeding (p-value 0.001) (p-value 0.009) (group 3). Conclusion: Magnesium sulfate and total body cooling is a safe therapy that enhances short-term clinical and radiological outcomes for the treatment of HIE infants.

Keyword: Infants with Hypoxic-Ischemic Encephal opathy, Magnesium Sulfate, Treatment, Whole Body Cooling

INTRODUCTION:

In full-term newborns, hypoxic-ischemic injury continues to be a significant contributor to perinatally acquired brain damage. The presence of neonatal encephalopathy is the best indicator of mortality and long-term outcome following perinatal injury. The probability of death is less than 10% if substantial encephalopathy is present, and up to one-third of survivors may have physical impairments. Mortality rates are higher (up to 60%) and most, if not all, survivors have disabilities with severe encephalopathy. High-quality randomized controlled trials have demonstrated the efficacy and safety of induced hypothermia in the treatment of post-asphyxial encephalopathy. Moreover, it lowers the risk of death and disability between the ages of 18 and 22 months.

Infants with moderate hypoxic-ischemic encephalopathy (HIE) or those born before 35 weeks should not be cooled, according to the available research. The acquired syndrome known as hypoxic-ischemic encephalopathy (HIE) is characterized by signs of acute brain injury in the clinical, laboratory, and radiological realms[(1)]. In wealthier nations, Per 1,000 live babies, two suffer from perinatal asphyxia, but when maternal and infant care is subpar, it affects ten times more people in developing nations. Between 15 and 20 percent of asphyxiated newborns will pass away during the neonatal period, and about 25 percent of those who survive will have long-term neurological problems[(2)].

Primary and secondary energy failure are two phases of pathologic processes that go along with HIE. Primary energy failure is characterized by significant tissue acidity, decreased cerebral blood flow, and oxygen deficiency[(3)]. In addition to excitatory brain neurotransmitters, protein synthesis, oxidative stress, inflammation, apoptosis, and other changes in growth factors, secondary energy failure comprises several pathophysiologic effects[(4)]. Between primary and secondary energy failure, there is a latent phase that correlates to a therapeutic window for the initiation of neuroprotective therapy of approximately six hours[(5)].

One neuroprotective therapy that affects several processes in the circumstances leading to brain injury is hypothermia of the brain. A small dip in brain temperature (between 1 and 6°C) in infants is associated with greater energy preservation in the brain during and right after ischemia. The stability of protein synthesis, reduction of free oxygen radicals, regulation of microglial activation and cytokine production, attenuation of excitatory neurotransmitter release, and attenuation of apoptosis are some of the additional neuroprotective effects of brain hypothermia[6]. To maximize the benefits of therapeutic hypothermia (TH), reduce infant brain damage, and create more neuroprotection, additional neuroprotective therapies should be used; numerous studies indicate the efficacy and[7-9] Infusions of dopamine (5 ug/kg per minute) and magnesium sulphate (250 mg/kg per day for three days) was used as an adjuvant therapy to treat TH given postnatally after birth asphyxia are linked to good neurodevelopmental outcomes because they have anticonvulsant and plasma membrane stabilizing effects as well as actions at N-methyl D-aspartate (NAMDA) glutamate receptors that are non-competitive antagonistic. Combination therapy, such as MS and TH, enhance results and have stronger synergistic neuroprotective benefits[10-12]. Hence.

AIM OF THE STUDY:

The objective of the current study was to evaluate the effects of whole-body cooling and magnesium sulfate on infants with hypoxic-ischemic encephalopathy treatment

PATIENTS AND METHODS:

39 neonates who met the physiological and neurological inclusion criteria between February 2022 and July 2022 were studied as part of an interventional, randomized, controlled study at the Sohag NICU (neonatal intensive care unit) University Hospital. Infants under 36 weeks of gestation admitted to the NICU who had at least one of the following meeting the physiological criteria: A five-point Apgar score at five minutes after delivery; ten minutes after birth, the need for resuscitation as endotracheal ventilation or a mask; and Acidosis with a pH 7.1 or a base deficit 16 mmol/L 60 minutes after birth; indications of fetal distress before to delivery, such as meconium-stained amniotic fluid, tachycardia >160 bpm, or bradycardia 100 bpm. Alterations in consciousness (such as lethargy, stupor, or coma) and at least one of the following were considered neurological criteria. Clinical seizures, altered pupillary reflexes, an abnormal oculomotor reflex, a lack of sucking or a lack of the Moro reaction, hypertonia, and other symptoms. Preterm children, children with congenital defects, and children whose mothers had taken drugs like phenobarbitone or pethidine that produced neonatal depression were excluded from the study.

Study Population and Sampling Size:

All neonates admitted to the Sohag University Hospital's NICU in Egypt during the research period with moderate to severe HIE were included. Before being divided into two subgroups and randomly assigned to mild, moderate, or severe HIE, the patients were first classified into two subgroups. The researchers separated the neonates into three groups depending on the severity of HIE, the priority of admission, and the availability of NICU rooms using random number tables generated by a computer based on the inclusion and exclusion criteria. The attending neonatologists and the NICU nurses were unaware of this

randomization.

Data Collection Tools:

Complete blood counts, serum urea, creatinine, magnesium, calcium, and potassium levels, as well as blood glucose levels, were measured. Detailed maternal, obstetric, and neonatal histories were also obtained. A thorough clinical examination was also conducted, including a neurological test.

Patients:

Neonatal HIE patients treated with whole-body cooling for 72 hours starting within 6 hours of delivery made up Group 1 (n = 13). Group 2 (n = 13) had HIE newborns who received preventive three days of intravenous MS (250 mg/kg) and dopamine (5 g/kg/min) over an hour, as well as total body freezing administered within six hours of birth for 72 hours. HIE newborns were included in Group 3 (n = 13), which acted as a control group and received supportive care. Due to a shortage of resources, the availability of spaces for newborns, and the cooling device in our NICU (which relied entirely on gel mattresses and passive cooling), the standard treatment (supporting measures) was the only approach used for the management of HIE cases in the control group. In addition, despite the positive effects of TH, management of these cases used standard treatment due to there is not enough nursing assistant staff to closely monitor and follow up on these patients. With an emphasis on maintaining oxygen saturation, blood pressure, normal blood gases, fluid balance, and renal functions, as well as controlling seizures, hypoglycemia, and jaundice, all babies were thoroughly watched and treated in accordance with conventional practices. At six hours of delivery, cooling began, and it persisted for 72 hours. The target temperature for cooling during hypothermic therapy and rewarming must be 33 to 34°C; the temperature was continuously monitored and recorded every hour.

The goal was to reach the desired temperature one hour after the cooling process began. Passive cooling was utilized to start TH, but after 30 minutes Active cooling was used if the temperature did not drop below 35°C. The infant was kept naked in an open incubator at room temperature with the radiant heater turned off, while active cooling was achieved by using a cold mattress at a temperature of about 10°C. The cooling mattress or packs are removed if the baby's temperature falls below 33°C. As if that weren't enough, the radiant heater is activated at its lowest level until the temperature hits 33 °C.[(14)]. After 72 hours of TH, a slow rewarming to a temperature of 37°C was carried out.

Temperature increase in the patient was limited to 0.5°C each hour using a radiant heater that was temperature-controlled to achieve this. 15 Both clinical and radiological evaluations were used to evaluate the cases. The Thompson and Sarnat scoring systems were used to conduct a clinical examination. Magnetic resonance imaging (MRI)16 pictures were used to evaluate radiological evaluation on the neonates when they were stable enough to be taken safely to the MRI scanner. 17 It was noted when feeding was initiated when mechanical ventilation and respiratory assistance were used, when neurological findings were noted on an MRI, and when convulsions and neurological states were prevalent.

Ethical consideration:

The Sohag University Hospital's local ethical committee in Egypt accepted the research. Every participant's mother or a guarantee was obtained before participat-ion and after being informed of the purpose of the study at the time of

enrollment.

Statistical Analysis

Using IBM SPSS Statistics SPSS Inc., version 25; for Windows, Microsoft ran a descriptive statistical study. To evaluate the normal value distribution, the Shapiro-Wilk test was used. The information was gathered, examined, coded, and entered. The descriptive analysis used in statistical approaches comprised the mean, standard deviation, number, and Pearson Chi-square test %. A one-way ANOVA test and the post hoc least significant difference method were used to determine the significance between groups for classified data and parametric variables, respectively. Statistical significance was set at $p < 0.05$.

RESULTS:

Table 1 Demographic data of the studied groups

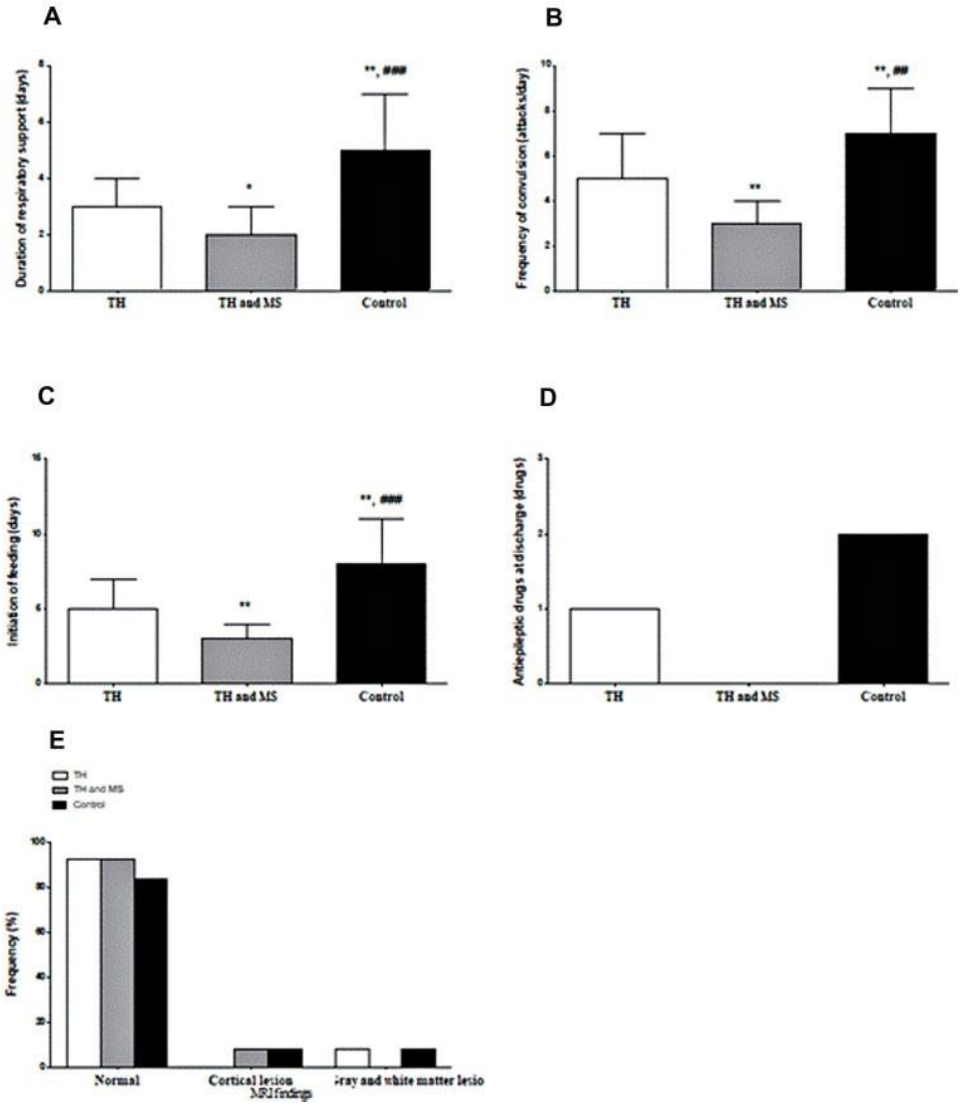
Parameters	TH group(n 13)	TH and MS group (n 13)	Control group(n 13)	p-Value
Gender				
Males	7 (53.84%)	5 (38.46%)	8 (61.54%)	0.43
Females	6 (46.16%)	8 (61.54%)	5 (38.46%)	
Birth weight (kg)	3.22 0.61	3.33 0.53	3.45 0.69	0.414
Gestational age (weeks)	38.33 1.36	38.67 1.55	38.1 1.79	0.206
Mode of delivery				
Normal vaginal delivery	5 (38.46%)	7 (53.84%)	6 (46.16%)	0.947
Cesarean section	4 (30.76%)	4 (30.76%)	4 (30.76%)	0.923
Forceps delivery	2 (15.38%)	—	1 (7.69%)	0.987
Ventose delivery	1 (7.69%)	1 (7.69%)	2 (15.38%)	0.786
Assisted breech	1 (7.69%)	1 (7.69%)	—	0.465

Table 1 displayed the demographic differences between the groups under study. In the neonates with hypothermia group, there were six (53.84%) male cases and six (46.16%) female cases, and there were seven (38.46%) male cases and five (61.54%) female cases in the hypothermia and MS group, but there was no significant difference between the groups in the control group (p 14 0.431). In the hypothermia, hypothermia with MS, and control groups, there were no appreciable differences in birth weight or gestational age (3.22 0.61kg, 3.33 0.53 kg, and 3.45 0.69 kg, respectively, p 0.414). (38.33 1.36; 38.67 1.55; and 38.1 1.79weeks, respectively; p 0.206). The techniques of delivery for the hypothermia; hypothermia and MS and control groups were vaginal (38.46, 53.84, and 46.16%, p 0.947), CS (30.76, 30.76, and 30.76%, p 0.913), forceps (15.38%, 7.69%, p 0.987), ventose (7.69, 7.69, and 15.38%, p 0.786) and aided breech (7.69 and 7.69 %, p 0.465).

Table 2 Risk factors for neonates with hypoxia ischemic encephalopathy during pregnancy.

Pregnancy risk factors	TH group(n 13)	TH and MS group (n 13)	Control group(n 13)	p-Value
Eclampsia	1 (7.69%)	1 (7.69%)	2 (15.38%)	0.766
Pre-eclampsia	5 (38.46%)	4 (30.76%)	1 (7.69%)	0.018
Previous stillbirth	1 (7.69%)	1 (7.69%)	—	—
Cord prolapse and placental insufficiency	1 (7.69%)	1 (7.69%)	2 (15.38%)	0.767
Antepartum hemorrhage	2 (15.38%)	1 (7.69%)	2 (15.38%)	0.017
Premature rupture of membrane.	2 (15.38%)	2 (15.38%)	1 (7.69%)	0.813
Prolonged 2nd stage of labor	2 (15.38%)	3 (23.07%)	5 (38.46%)	0.016

The risk factors for newborns with HIE during pregnancy are shown in Table 2. Pre-eclampsia, antepartum hemorrhage, and protracted second stage of labor were significantly different among the groups under study (p 0.018, p 0.017, p 0.016, respectively).



The Fig. Short-term outcomes among the studied groups; ᵠSignificance versus TH group; #Significance versus TH and MS group

The MRI results and short-term outcomes for each group under study are shown in Fig. 1. There were statistically significant differences in the duration of respiratory support (p 0.022, p 0.001, and p 0.005, respectively), frequency of convulsions (p 0.005, p 0.002, and p 0.002, respectively), initiation of feeding (p 0.005, p 0.001, and p 0.007, respectively), and antiepileptic medications at discharge between the hypothermia and MS group and the hypothermia and control groups (p 0.001; p 0.006, and p 0.032, respectively). (93%) of the hypothermia group's MRI results were normal, and one case (7.69%) had grey and white matter lesions;

Findings were normal in (93%) of the hypothermia with MS group and cortical in one case (7.69%), while in the control group, they were normal in (84%) of the group, cortical in (7.69%), and grey and white matter lesion (7.69%), with no statistically significant difference between the different findings (normal, cortical lesion, and grey and white matter lesion) in the different groups (p 0.306, p 00.856, and p 0.817, respectively).

DISCUSSION:

The care for neonates with HIE is hypothermia, however, since hypothermia does not completely protect the nervous system, improved results can occur by adding a pharmaceutical drug. MS is a prime example of one of these drugs used in newborns that has neuroprotective properties.[18] This prospective intervention study's goal was to Examine the differences between whole body cooling and whole body cooling's immediate consequences of neonates with HIE admitted to the NICU of the hospital at Sohag University who met the study's inclusion criteria paired with MS as a neuroprotective agent.

Across the three study groups, there was an insignificant gender difference in this study. Meanwhile, the number of males (n 14 22, 61.11%) was higher than that of females, with six (50%) of the cases in the group of neonates with hypothermia being males as well as six (50%) females, whereas in the group with MS and hypothermia, there were five (41.7%) girls and seven (58.3%) males, compared to nine (75.0%) males and three (25.0%) females in the control group. In 144 newborns with prenatal asphyxia studied by Siegel et al.[19] in Pakistan, 68.8% of the patients were male and 31.3% were female. According to this study, the male sex has a negative impact on a newborn's prognosis in situations of prenatal hypoxia.[19]

Caspase-dependent and -independent cell death pathways are both stimulated by cerebral ischemia. Male stroke patients experience cell death that is not dependent on caspase as a result of the release of apoptosis-inducing chemicals from the mitochondria.

Infants' second stages of labor were prolonged by 25.0%, women experienced pre-eclampsia (22.22%), there were 13.89% antepartum hemorrhages, 13.89% premature membrane ruptures, and 11.11% had cord prolapse and placental insufficiency, (11.11%) had eclampsia, and (5.56%) had a history of stillbirth. Antepartum hemorrhage, the protracted second stage of labor, and preeclampsia all showed a substantial difference across the various study groups (p 0.016, p 0.017, and p 0.019).

According to Torbenson et al.[20], the presence of meconium-stained amniotic fluid and risk factors for the development of HIE included the labor stage. As opposed to what we discovered, Hashim et al,[21], study found that a significantly higher risk was connected to a protracted membrane rupture, which is a risk factor

for fetal sepsis and connected to a decline in the fetal acid-base status. A ruptured uterus, placental abruption, moderate-to-heavy meconium-stained amniotic fluid, and cesarean birth were all identified as independent intrapartum risk factors for HIE in newborns by Peebles et al[22]. In the HIE group, 70.3% of women had an intrapartum risk factor, compared to 29.6% in the non-HIE group.

Our research found across the several delivery methods, there is no statistically significant difference. among the several investigated groups of HIE, regardless of the mode of delivery. The majority of births among the HIE group involved normal vaginal delivery (n = 16, 44.44%), followed by cesarean sections (n = 11, 30.56%), ventose births (n = 4, 11.11%), forceps births (n = 3, 8.33%), and finally aided breech births (n = 2, 5.56%).

The typical vaginal birth, as described by Hill23 and Badawi et al.,[24] is linked to HIE, which is consistent with the findings of this investigation. According to Dongol et al[25], the majority of vaginal births are linked to perinatal and intrapartum hypoxia. Seyal and Hanif[26], on the other hand, noted that the majority of newborns with birth asphyxia were delivered via cesarean section. This may be explained by internal hospital protocols that favor CS or by the use of CS as the preferred method of birth following unsuccessful attempts at regular vaginal delivery.

The findings revealed In the three groups under study, there was a statistically significant difference in the incidence and frequency of clinical seizures (p 0.001), the duration of respiratory support (p 0.001), and the time at which enteral feeding was started (p 0.009), all of which were determined by the short-term outcomes among the study groups. According to our findings, the hypothermia with MS group required less mechanical ventilation and respiratory assistance than the hypothermia alone group, which was also less than the control group. Also, the group that underwent hypothermia with MS took a shorter time to begin feeding than the group that received hypothermia only. The incidence of clinically discernible seizures was significantly influenced by TH, according to a meta-analysis of five investigations on infants with HIE.[27,28]. The therapy when administered shortly after delivery, postnatal intravenous MS (250 mg/kg/dose,[24] hours between three doses), in neonates with severe birth asphyxia, according to Sajid et al[29], improved neurological outcomes at discharge. Similar to the current investigation, Neonates with moderate to severe HIE had a lower chance of mortality, according to research by Abate et al.,[30]. Infants with HIE were less likely to die when whole-body and selective head cooling was used. Moreover, therapy is especially beneficial for low-income countries.

In a porcine model of term neonatal encephalopathy, The neuroprotective effects of MS for 48 hours (180 mg/kg bolus followed by 8 mg/kg/h infusion), TH for 12 hours (33.5°C), and TH alone were examined by Lingam et al.[31]. They observed an increase in oligo-dendrocytes (p = 0.002) and a general decrease in cell death (p = 0.010) in MS + TH compared to TH alone. While this was going on, there was no improvement in the (Lac/NAA; PCr/Pi; NTP/epp) Magnetic resonance spectroscopy or amplitude-integrated electroencephalography recovery (p 0.084 or p > 0.05) at 48 hours. A trial by Prakash32 involved giving an MS infusion or a placebo within 48 hours of birth to 60-term asphyxiated neonates. A 250 mg/kg/dose (1 mL/kg/dose in 20 mL of 5% dextrose solution) MS infusion was administered within six hours after birth. A further two dosages were administered at

24-hour intervals. According to the author, 25/36 infants in the magnesium group (69%) and 27/33 controls (82%) with moderate and severe HIE experienced clinical seizures during NICU stay. Of the 24 infants (96%) in the MS group who had seizures, only 20 (74%) in the placebo group were seizure-free (p 0.020).

When compared to the placebo group, the MS group's seizures were controlled for 36.5 hours as opposed to 55 hours earlier (p 0.020). Upon discharge, Both the MS group's two infants and the placebo group's three neonates required anticonvulsants. The survival of asphyxiated neonates and neonates with encephalopathy is increased, in accordance with Okonkwo and Okolo[33], by postnatal administration of MS, either by itself or in conjunction with respiratory assistance. Using full-term newborns who had had severe perinatal hypoxia, Bhat et al., ten studies found that postnatal MS treatment improved neurological outcomes at discharge. Early (within 6 hours) postnatal intravenous MS infusion has been shown to improve short-term outcomes for newborns with perinatal hypoxia, according to Sreeni-Vasa et al.[34].

The MRI patterns of brain injury fluctuate depending on the age of the brain at the time of the lesion, its severity, and how long it lasted. In neonates with encephalopathy, MRI imaging is used as an early indicator of the future appearance of neurological disorders, according to Aun et al.[35]. It is a sensitive method for recognizing various encephalopathy patterns in newborns. MRI can be used in interventional trials designed to reduce harm and enhance neuro-developmental outcomes, according to Rutherford et al.[36] after prenatal brain injury. It is a good predictor of outcome. The findings of this study showed a relationship between the use of MS and whole-body cooling in reducing MRI-detected brain damage that is indicative of HIE.[37] Consequently, (88.89%) of the 36 cases in the current study that had MRI scans revealed normal results even though they met the criteria for hypoxic encephalopathy. Whereas in the hypothermia group, (92.7%) had normal MRI results and (8.3%) had grey and white matter lesions. (92.7%) of the hypothermia with MS group had normal MRI results, and one case (8.3%) had a cortical lesion. Normal MRI was seen in (83.4%) of the control group, cortical lesions were seen (in 8.3%), and grey and white matter lesions were seen in (8.3%). This confirms our hypothesis that cooling may have reduced the severity of hypoxic brain injury, whether or not prophylactic MS was used. According to Cheong et al.[38], neonates that received hypothermia experienced less brain damage on T1- and T2-weighted MRI scans. Regardless of the use of hypothermia therapy, abnormal MRI is predictive of long-term outcomes in moderate to severe HIE.

Conclusion:

Whole-body cooling is a simple and widely accessible strategy that has become to be the recommended course of care for newborns with HIE. It is safe, effective, and affordable. The length of the hospital stay is greatly reduced when MS is added to cooling therapy for HIE. Convulsions are also less common, feeding can begin earlier, and less anticonvulsant medication is used. To ascertain the long-term outcomes, follow-up of HIE cases treated with TH is strongly advised.

Conflict of Interest:

No Conflict of Interest

REFERENCES:

1. **Martinello K, Hart AR, Yap S, Mitra S, Robertson NJ.** Management and investigation of neonatal encephalopathy: 2017 update. Arch Dis Child Fetal Neonatal Ed 2017;102(04): F346–F358
2. **Odd D, Heep A, Luyt K, Draycott T.** Hypoxic-ischemic brain injury: planned delivery before intrapartum events. J Neonatal Perinatal Med 2017; 10 (04): 347–353
3. **Dixon BJ, Reis C, Ho WM, Tang J, Zhang JH.** Neuroprotective strategies after neonatal hypoxic-ischemic encephalopathy. Int J Mol Sci 2015; 16(09):22368–22401
4. **Arteaga O, Álvarez A, Revuelta M, Santaolalla F, Urtasun A, Hilario E.** Role of antioxidants in neonatal hypoxic–ischemic brain injury: new therapeutic approaches. Int J Mol Sci 2017; 18(02):265
5. **Laptook AR, McDonald SA, Shankaran S, et al;** Extended Hypothermia Follow-up Subcommittee of the National Institute of Child Health and Human Development Neonatal Research Network. Elevated temperature and 6- to 7-year outcome of neonatal encephalopathy. Ann Neurol 2013;73(04):520–528
6. **Wassink G, Davidson JO, Dhillon SK, et al.** Therapeutic hypothermia in neonatal hypoxic-ischemic encephalopathy. Curr Neurol Neurosci Rep 2019;19(02):2
7. **Nonomura M, Harada S, Asada Y, et al.** Combination therapy with erythropoietin, magnesium sulfate and hypothermia for hypoxic-ischemic encephalopathy: an open-label pilot study to assess the safety and feasibility. BMC Pediatr 2019;19(01):13
8. **Rahman SU, Canpolat FE, Oncel MY, et al**. Multicenter randomized controlled trial of therapeutic hypothermia plus magnesium sulfate versus therapeutic hypothermia plus placebo in the management of term and near-term infants with hypoxic-ischemic encephalopathy (The Mag Cool study): a pilot study. J Clin Neonatol 2015; 4 (03):158
9. **El Farargy MS, Soliman NA.** A randomized controlled trial on the use of magnesium sulfate and melatonin in neonatal hypoxic-ischemic encephalopathy. J Neonatal Perinatal Med 2019; 12(04):379–384
10. **Bhat MA, Charoo BA, Bhat JI, Ahmad SM, Ali SW, Mufti MU.** Magnesium sulfate in severe perinatal asphyxia: a randomized, placebo-controlled trial. Pediatrics 2009; 123 (05):e764–e769
11. **Lingam I, Robertson NJ.** Magnesium as a neuroprotective agent: a review of its use in the fetus, term infant with neonatal encephalopathy, and the adult stroke patient. Dev Neurosci 2018; 40(01):1–12
12. **Zhou KQ, Davidson JO, Bennet L, Gunn AJ.** Combination treatments with therapeutic hypothermia for hypoxic-ischemic neu- protection. Dev Med Child Neurol 2020;62(10):1131–1137
13. **Shalak LF, Laptook AR, Velaphi SC, Perlman JM.** Amplitude-inte- grated electroencephalography coupled with an early neurologic examination enhances the prediction of term infants at risk for persistent encephalopathy. Pediatrics 2003;111(02):351–357
14. **Badr-El Din MM, Abougabal AM, Saad KM, Abdel-Salam HR.** Effect of erythropoietin as adjunctive therapy with whole-body cooling for treatment of hypoxic-ischemic encephalopathy in newborns. Alex J Pediatrics 2017; 30 (02): 45–52
15. **Azzopardi D, Brocklehurst P, Edwards D, et al; TOBY Study Group.** The TOBY Study. Whole body hypothermia for the treatment of perinatal asphyxial encephalopathy: a randomized controlled trial. BMC Pediatr 2008; 8 (01):17
16. **Massaro AN, Murthy K, Zaniletti I, et al.** Short-term outcomes after perinatal

hypoxic-ischemic encephalopathy: a report from the Children's Hospitals Neonatal Consortium HIE focus group. J Perinatol 2015;35(04):290–296

17. **Zanelli S, Buck M, Fairchild K.** Physiologic and pharmacologic considerations for hypothermia therapy in neonates. J Perinatol 2011;31(06):377–386
18. **Valera IT, Vázquez MDC, González MDR, et al.** Erythropoietin with hypothermia improves outcomes in neonatal hypoxic-ischemic encephalopathy. J Clin Neonatol 2015;4(04):244–249
19. **Siegel C, Li J, Liu F, Benashski SE, McCullough LD.** miR-23a regulation of X-linked inhibitor of apoptosis (XIAP) contributes to sex differences in the response to cerebral ischemia. Proc Natl Acad Sci U S A 2011;108(28):11662–11667
20. **Torbenson VE, Tolcher MC, Nesbitt KM, et al**. Intrapartum factors associated with neonatal hypoxic-ischemic encephalopathy: a case-controlled study. BMC Pregnancy Childbirth 2017;17(01): 415
21. **Hashim N, Naqvi S, Khanam M, Jafry HF.** Primiparity as an intra- partum obstetric risk factor. J Pak Med Assoc 2012;62(07):694–698
22. **Peebles PJ, Duello TM, Eickhoff JC, McAdams RM**. Antenatal and intrapartum risk factors for neonatal hypoxic-ischemic encephalopathy. J Perinatol 2020; 40(01):63–69
23. **Hill A.** Current concepts of hypoxic-ischemic cerebral injury in the term newborn. Pediatr Neurol 1991;7 (05): 317–325
24. **Badawi N, Felix JF, Kurinczuk JJ, et al.** Cerebral palsy following term newborn encephalopathy: a population-based study. Dev Med Child Neurol 2005;47(05):293–298
25. **Dongol S, Singh J, Shrestha S, Shakya A.** Clinical profile of birth asphyxia in Dhulikhel Hospital: a retrospective study. J Nepal Paediatr Soc 2010;30(03):141–146
26. **Seyal T, Hanif A**. Factors related to adverse outcome in asphyxiated babies. Ann of King Edward Med Univ 2009;15(04):180–180
27. **Marks K, Shany E, Shelef I, Golan A, Zmora E.** Hypothermia: a neuroprotective therapy for neonatal hypoxic-ischemic encephalopathy. Isr Med Assoc J 2010;12(08):494–500
28. **Jacobs SE, Morley CJ, Inder TE, et al;** 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 2011;165(08):692–700
29. **Sajid NK, Junaid M, Ahmed S.** Therapeutic efficacy of magnesium sulphate on the neurological outcome of neonates with severe birth asphyxia. J Univ Med Dent Coll 2018;9(04):1–5
30. **Abate BB, Bimerew M, Gebremichael B, et al.** Effects of therapeutic hypothermia on death among asphyxiated neonates with hypoxic-ischemic encephalopathy: a systematic review and meta-analysis of randomized control trials. PLoS One 2021;16(02): e0247229
31. **Lingam I, Meehan C, Avdic-Belltheus A, et al.** Short-term effects of early initiation of magnesium infusion combined with cooling after hypoxia-ischemia in term piglets. Pediatr Res 2019;86(06): 699–708
32. **Prakash R.** Effect of postnatal magnesium therapy on neonatal seizure in infants with moderate to severe hypoxic-ischemic encephalopathy: A posthoc subgroup analysis. Int J Contemp Pediatrics 2016; 3 (04):1425–1429
33. **Okonkwo IR, Okolo AA.** Pediatrics & neonatal care. Magnesium 2018;30:31
34. **Sreenivasa B, Lokeshwari K, Joseph N.** Role of magnesium sulphate in

management and prevention of short-term complications of birth asphyxia. Sri Lanka J Child Health 2017;46(02): 148–151

35. **Aun AE-AK, Hassan HA, Ali WI, Ataky MMA.** Transcranial ultra sound in comparison to MRI in the evaluation of hypoxic-ischemic injury in neonates. Egypt J Hosp Med 2019;74(04):842–852
36. **Rutherford M, Biarge MM, Allsop J, Counsell S, Cowan F.** MRI of perinatal brain injury. Pediatr Radiol 2010;40(06):819–833
37. **Chao CP, Zaleski CG, Patton AC.** Neonatal hypoxic-ischemic encephalopathy: multimodality imaging findings. Radiographics 2006;26(Suppl 1):S159–S172
38. **Cheong JL, Coleman L, Hunt RW, et al;** Infant Cooling Evaluation Collaboration. Prognostic utility of magnetic resonance imaging in neonatal hypoxic-ischemic encephalopathy: a substudy of a randomized trial. Arch Pediatr Adolesc Med 2012;166(07): 634–640

تأثيرات تبريد الجسم بالكامل وكبريتات المغنيسيوم على الرضع المصابين باعتلال الدماغ بنقص التأكسج

رانيا رفعت عبد القادر عطية ، منال محمد أحمد عايد , سعيدة حمدان احمد الجدعاني

[1]قسم علم وظائف الأعضاء بكلية الطب جامعة الزقازيق وبقسم العلوم الطبية الأساسية بكلية العلوم الطبية التطبيقية

[2] قسم تمريض الأطفال ، كلية التمريض ، جامعة سوهاج ، مصر

[3]قسم العلوم الأساسية ، كلية العلوم الطبية التطبيقية ، جامعة الباحة ، الباحة ، المملكة العربية السعودية

في حديثي الولادة المصابين باعتلال الدماغ بنقص التأكسج المعتدل إلى الشديد (HIE) ، يقلل انخفاض درجة الحرارة العلاجي - (TH) إما عن طريق التبريد المستهدف للرأس أو تبريد الجسم بالكامل - من تلف الدماغ ، ويوفر الحماية العصبية ، ويقلل من معدلات الوفيات ، خاصة إذا بدأ في الست ساعات الأولى بعد الولادة. علاوة على ذلك ، فإن العلاج المساعد مثل إدارة كبريتات المغنيسيوم (MS) يوفر حماية عصبية متزايدة. كان الهدف من الدراسة التدخلية العشوائية الخاضعة للرقابة هو تقييم الآثار قصيرة المدى لاستخدام TH بمفرده أو بالتزامن مع مرض التصلب العصبي المتعدد كدواء وقائي للأعصاب لعلاج الأطفال حديثي الولادة مع .HIE الهدف: تقييم آثار الجسم كله التبريد وكبريتات المغنيسيوم عند الرضع الذين يعانون من اعتلال الدماغ بنقص التأكسج. المرضى والأساليب: تم تسجيل 39 مولودًا حديثًا استوفوا معايير HIEوولدوا في وحدة العناية المركزة لحديثي الولادة في مستشفى جامعة سوهاج في الدراسة. تم تقسيمهم بالتساوي بين المجموعات الثلاث ؛ خلال الست ساعات الأولى من الحياة ، تلقت المجموعة 1 (رقم 13) تبريد الجسم بالكامل باعتباره العلاج الوحيد ؛ المجموعة 2 (العدد 13) تلقت تبريد الجسم بالكامل بالإضافة إلى التصلب المتعدد كعلاج مساعد ؛ والمجموعة 3 (ن 13) تلقت تدابير الرعاية الحادة الداعمة كعنصر تحكم. النتائج: بمقارنة مجموعة (TH plus MS المجموعة 2) بالمجموعات الأخرى التي تديرها) TH المجموعة 1) أو العلاج الداعم ، كان لدى مجموعة TH plus MS) المجموعة 2) نتائج أفضل على المدى القصير بشكل ملحوظ كما تم قياسها من خلال فترة قصيرة من الجهاز التنفسي الدعم والتهوية الميكانيكية (القيمة الاحتمالية 0.001) ، وانخفاض حدوث التشنج (القيمة الاحتمالية 0.001) ، والبدء المبكر في التغذية (القيمة الاحتمالية 0.009). (المجموعة 3). الخلاصة: إن تبريد الجسم بالكامل بالإضافة إلى التصلب المتعدد كعلاج مساعد لعلاج حديثي الولادة HIE هو علاج آمن يحسن النتائج قصيرة المدى سريريًا وشعاعيًا.