Nauka praktyce / Science for medical practice

OPIS PRZYPADKU / CASE REPORT
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Therapeutic hypothermia in children post cardiac arrest – single center experience

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Abstract

Background. Therapeutic hypothermia, defined as controlled body cooling below physiological temperature, is well recognized and recommended in post resuscitation management. It aims for protection of brain and heart, which are most susceptible to anoxic tissue damage leading to poor clinical outcome and worsening of personal and social functioning of affected individuals. According to current clinical knowledge therapeutic hypothermia is effective and safe management method improving quality of life and intellectual functions of cardiac arrest survivors, as compared to traditional intensive care approach. Current guidelines imply induced hypothermia in adult cardiac arrest patients in post resuscitation care and in asphyxiated neonates, predestined to development of anoxic-ischaemic encephalopathy. There are very few publications referring to use of therapeutic hypothermia in children below the age of 18 [1]. ***Case report.*** We describe 4 children who suffered cardiac arrest treated in our institution and managed by therapeutic cooling in post resuscitation care. *Anestezjologia i Ratownictwo 2020; 14: 147-152.*

Keywords: child, cardiac arrest, therapeutic hypothermia, anoxic-ischaemic encephalopathy

Introduction

Delayed post cardiac arrest sequelae of deep hypoxia in all age groups are related to severe brain damage and may lead to profound worsening of functional abilities and social exclusion [2,3]. Effective CPR (cardiopulmonary resuscitation) leading to ROSC (return of spontaneous circulation) is only a first stage in treatment. Quality of life and individual health depend on post-resuscitation care, focused on quick restoration of normal hemodynamic parameters and full brain function [3,4]. According to an up-to-date research mild therapeutic hypothermia (MHT), e.g. controlled full body cooling below physiologic temperature, proves to be brain and heart protective and is accepted as safe and effective method of good clinical prognosis for asphyxiated newborns in perinatal period and in adult cardiac arrest survivors [2,4,5]. Patients who have not been not asphyxiated neonates and those below the age of 18 are not proved to benefit from this method. In this age groups MHT, although accepted, is considered to be only of experimental value due to a lack of sufficient clinical data. There is a limited number of publications referring to the use of MHT in children in worldwide medical literature.

Cases report

Children were admitted to Pediatric and Neonatal Intensive Care Unit. Our PNICU is a third reference

Table I. Patient's demographics

	Patient 1	Patient 2	Patient 3	Patient 4
Gender	male	male	female	female
Age at cardiac arrest	3 hours	24 days	32 days	6 y and 3 months
Site of cardiac arrest	hospital	hospital	home	care facility
Cause of cardiac arrest	unknown	unknown	infection	strangulation
Witness at cardiac arrest	both parents	ward nurse and mother	both parents	unattented
Time to CPR	unknown	< 1 min	approx. 8min	approx. 7 min.
Length of CPR (performed by)	20 min (neonatologists)	20 min (pediatricians and anaesthetist)	20 min (parent and EMS)	2 min (parent and ward nurse)
Resuscitation drugs	epinephrine (4 doses) bicarbonate (2doses)	epinephrine (3doses) bicarbonate (1dose)	no drugs	no drugs
GCS at ROSC	< 6	< 6	< 6	4
Breathing at ROSC	mechanical ventilation	mechanical ventilation	spontaneous/ insufficient	spontaneous/ insufficient
Time to arrival to our institution	2 hours	1 hour	1 hour	1 hour
Transport	neonatal	neonatal	EMS	EMS
Temperature control in transport	passive cooling	passive cooling	active warming	active warming
Perinatal history	G1P1 gestational age 41 weeks vaginal delivery Apgar score 10	G1P1 gestational age 40 weeks emergency cesarean Apgar score 9 Toxo IgG 532U/l Toxo IgM neg	G1P1 gestational age 37 weeks vaginal delivery Apgar score 10	irrelevant
Past medical history	none	none	4 days history of upper airways infection and exertion on feeding	none
Family history	none	mother's Toxo IgM significant of infection	none	none

level facility with 4 neonatal and 7 pediatric intensive care beds available 24/7 for children in our region. Informed consent was obtained from parents before MHT was initiated. Demographic and clinical data are summarized in tables 1, 2 and figure 1.

Patients 1, 2 and 3 were assessed as mild in Sarnat scale. Patient 4 was assessed by GCS only and he scored 4 points. In further examination patients 1, 2 and 3 were subjected to aEEG analysis as per 3rd stage of neonatal asphyxia assessment and qualified for MHT according to aEEG results by applied CFM Olympic Medical device Brainz Monitor (fig.1).

Patient 4 was assessed with clinical criteria and qualified for MHT according to adult criteria with all necessary exclusions but patient's age [6,7].

In patients 1, 2, 3 a selective head cooling with mild whole body hypothermia was applied by Olympic Cool-Cap System device according to standard neonatal procedure, e.g. with lowering of internal body temperature to 34-35°C level for 72 hours [2]. Continuous monitoring included aEEG (figure 1) and rectal temperature. Additional measurements included peripheral head skin at frontal region, peripheral abdominal skin and cooling head cap temperatures. We maintained cap temperature at adjustable range from 11-17.6°C.

In our 4th patient a non-invasive mild therapeutic hypothermia was applied by Tecotherm Neo cooling pad device according to standard adult procedure, e.g. with keeping an internal body temperature at 34-34.5°C for 24 hours [7]. Continuous monitoring of

Table II. Clinical data outcome

		Patient 1	Patient 2	Patient 3	Patient 4
Pupils		narrow, reaction to light uncertain	narrow, reaction to light uncertain	moderate, good reaction to light	fairly wide, reaction to light delayed
Muscle tone on admission		flacidity, generalised seizures	increased, single seizure episode	diminished, incoherent movement	increased, jerking, seizures
Blood analysis		high hypoxia biomarkers, clotting disorder, inflammatory markers increased	hypoproteinemia, high hypoxia biomarkers	high hypoxia biomarkers, severe metabolic acidosis, increase in inflammatory markers, anemia	high hypoxia biomarkers, metabolic acidosis, hyperglycemia
Chest x-ray		clear	clear	pneumonia	aspirational pneumonia
Cranial ultrasound / scan		brain oedema	subepependymal cysts	clear	clear
Vasopressors		dobutamine 5 mcg/kg/min	dobutamine 5 mcg/kg/min	none	none
Cardiac ultrasound assessment		post anoxic hypokinesis	post anoxic hypokinesis	not performed	post anoxic hypokinesis
ROSC-MHT initiation time		5 hours	3 hours	5 hours	3 hours
MHT duration		72 hours	72 hours	72 hours	24 hours
Rewarmed passively at a rate		0.4-0.6°C/1 h	0.4-0.6°C/1 h	0.3-0.6°C/1 h	0.5-0.9°C/1 h
Discharge		home	home	home	home
Neuro rehabilitation		Bobath therapy	supportive positioning	supportive positioning	special occupational therapy
Neurological outcome		satisfactory at 3y age	satisfactory at 3y age	satisfactory at 2,5y age	satisfactory after 1y
Length of therapy	PICU	16 days	7 days	11 days	11 days
	Pediatric	11 days	13 days	8 days	14 days
	summary	27 days	20 days	19 days	25 days

rectal as well as peripheral temperatures at frontal head and abdominal regions was performed.

All treatment sessions were uneventful, with patient being sedated and mechanically ventilated.

All patients were rewarmed passively up until normothermia was achieved. Patient number 4 required acetaminophen administration in order to control rewarming (table II) and to maintain normothermia in the following days.

Neurological status of patients in the course of treatment

- **Patient 1**

Prior to transportation post-arrest general seizures were controlled with phenobarbital in a standard dose, but after admission patient required increased doses up to 40 mg/kg/day. Patient was qualified for MHT on the ground of abnormal aEEG trace (figure 1) and seizure control was augmented with dexamethasone (0,5 mg/kg/day) on a 2nd day. After MHT protocol was completed and sedation stopped on a 3rd day, he was rewarmed, woken up and extubated on a 6th day. Non-invasive ventilation was continued to 12th day. Catecholamines were gradually reduced and switched off on a 10th day. Parenteral nutrition was continued accompanied by gastric tube enteral feeding until continuously stimulated sucking reflex enabled the boy to be bottle fed. On a day 20 a consulting cardiologist found no residual cardiovascular abnormality.

In serial head ultrasound a brain oedema was found at the beginning, followed by a threshold blood circulation and normal view on a day 21st. We performed head MRI under general anaesthesia on a day 15th and it revealed some abnormality in subcortical nuclei in both hemispheres, hyperemia and minimal

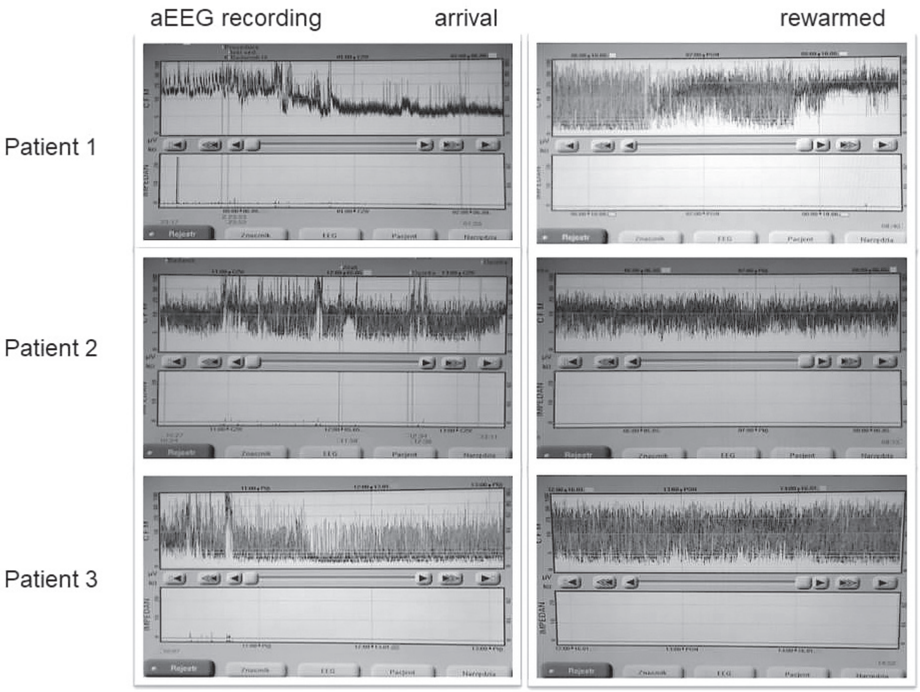

Figure 1. aEEG trace in patients 1, 2 and 3

bleed into lentiform nuclei and bilateral swelling of thalamus.

A patient was consulted by a paediatric neurologist on 12^{th} and 19^{th} day. First consultation revealed global muscular hypotonia, diminished limb reflexes, no Moro and Galant reflexes, no head elevation in traction. Second consultation showed positional asymmetry, abnormal traction and muscle tone, but this could have been attributed to a prolonged therapy with phenobarbital.

Regular NDT rehabilitation modo Bobath was started on day 20 and parents were educated on how to proceed with daily care.

A follow up at 14 months of age was preceded. The boy was cheerful, in full logical contact according to his age, with good understanding of a spoken language, trying to communicate verbally, mimicking simple gestures. His movements were simple and lacked coordination, but he was able to crawl and lift himself up on arm support. His muscle tone was diminished, especially at abdominal are and he showed signs of left lateralisation. Limb muscle tone was increased on right side with much worse functionality. His rehab continued with NDT modo Bobath and Vojta and neuro speech therapy was started. He was admitted for a week hospital rehabilitation course after which his movements greatly improved.

At 3 years of age the patient's development is satisfactory with minimal mobility deficits.

- **Patient 2**

He was extubated on day 5 and cardiac ultrasound confirmed normal hemodynamic function. Entetral and parenteral feeding was continued. From day 13 patient was on enteral bottle feeding only.

Cranial ultrasound sound revealed subependymal cysts (day 1^{st}, 3^{rd}) and confirmed IVH stage 1 in control on day 12. Neurological assessment confirmed left lateralisation, impaired head lift on shoulder traction and advised proper positioning and further consultation.

Due to a confirmed presence of subependymal cysts and perinatal history we performed lumbar function with cerebrospinal fluid analysis, toxoplasmosis screen inclusive. No abnormality was detected.

On follow-up 3 years post discharge the boy is developing well.

- **Patient 3**

She was extubated on day 8, followed by NIV and spontaneous breathing started on day 10. Enteral feeding started early by a gastric tube and she was on enteral bottle feeding from day 12.

First cranial ultrasound scan revealed no abnormality. Control (day 16) detected left side stage 3 IVH. Neurological consultation revealed right lateralisation, head deviation on shoulder traction, spinal asymmetry, no walking reflex. Parents were advised to proper positioning and neurological control.

On follow up 2,5 years post discharge the girl is developing well.

- **Patient 4**

Control head MRI was performed on day 4, with no abnormality detected. Sedation was stopped on day 6. The boy was extubated on day 7, with nasal cannula oxygen therapy continued for 2 days. Enteral feeding was started by a gastric tube and from day 9 the child was able to be spoon-fed with mild swallowing deficit.

Neurological examination on day 9 revealed: patient's confused, drowsy, not obeying commands, agitated, eye movements intact, facial movements symmetrical, muscle tone symmetrical, deep tendon reflexes normal, symmetrical, no meningeal or Babinski's signs. From day 11 the child was fully conscious, in full logical contact, without swallowing problems. He was a bit slow on obeying commands and his speech was slowed down. On repeated consultation no abnormality was detected and patient was advised for further general rehabilitation with a follow-up.

After 1 year post discharge the boy shows no neurological deficits and is developing well.

Summary

All patients have sustained a severe episode of brain asphyxia with cardiac arrest not related to perinatal history. MHT was initiated within 6 hours post anoxic incident in all cases, which met the inclusion criteria [2,5]. None of our patients met full neonatal stage I qualification criteria (postnatal age 1 hour, 10 min Apgar score < 5, umbilical blood pH ≤7,0 and BE >16 mmol/l, mechanical ventilation within 10 minutes post birth) [2].

Mild therapeutic hypothermia has been recognised as post cardiac arrest supportive therapeutic method in children in the past years [2,8]. Current guidelines advise its application in out-of-hospital cardiac arrest in adults in non-shockable arrest rhytms and in asphyxiated newborns. This is a recommendation issued by American Academy of Pediatrics, American Heart Association and European Resuscitation Council [3,4]. In Dec 2012 and Feb 2013 MHT was accepted as a basic therapeutic procedure and contracted by National Health Fund in Poland. Its application in post cardiac arrest children is also accepted [9,10].

We based our decision on neonatal stage II qualification criteria, e.g. aEEG trace in patient 2, 3 and in patient 1 on neonatal stage III qualification criteria (general seizures) [2,5]. Patient 4 was qualified according to adult criteria of GCS score and untreatable seizures. We experienced no hypothermia complications and neurological outcome was favourable in all cases.

Notable in 2 of our patients passive cooling was started as early as in the prehospital phase. These neonates were referred directly for selective cooling by a referring hospital and transported by our own neonatal transport team in a neonatal ambulance. Older patients were transferred by EMS and although with a known history ROSC post cardiac arrest no cooling means were initiated at this stage. This is probably due to a lack of general knowledge regarding the positive effect of cooling on post cardiac arrest patients and also lack of designated treatment protocols for patients other than out-of-hospital VF cardiac arrest victims and asphyxiated newborns. In some instances post cardiac arrest children are being warmed up and protected against a temperature loss. Some EMS protocols seem to respect and value a then revolutionary publication by Silverman et al published in 1958 discussing a detrimental effect of cold environment on a pediatric patient.These attitudes should now be abandonded and more modern knowledge about Mild Therapeutic Hypothermia for all age groups and how to start is as early as possible in all instances.

Conclusions

In decision making process in cardiac arrest children one should bear in mind that the primary guidelines were based on extrapolation of results obtained in adults and neonates. Individual indications and potential favourable outcome must be taken into account [4,5,8].

These factors are particularly important in perspective of other studies in which comparable results were achieved in post cardiac arrest adults treated with normothermia and target body temperature of 36°C [12].

Conflict of interest
None

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