

Induced hypothermia in comatose survivors of asphyxia: a case series of 14 consecutive cases

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Background: Induced hypothermia is widely used for comatose survivors of cardiac arrest. Other causes of hypoxic brain injury carry a poor prognosis when treated using traditional methods. At our hospital, hypothermia has also been used for the management of all comatose survivors of asphyxiation. The aim of the present study was to report the results of the management of these patients.

Methods: Hospital charts of all patients admitted unconscious after asphyxiation during a 7-year period were reviewed. This included patients after hanging, drowning, carbon monoxide intoxication and other gas intoxications. In all patients, hypothermia with a target temperature of 32–34 °C was induced with external or intravascular cooling for 24 h. The primary outcome was neurologic function at discharge.

Results: Fourteen male patients were treated with hypothermia, eight after hanging, three after drowning, two after carbon monoxide intoxication and one after methane

intoxication. All were deeply comatose (Glasgow Coma Score 3–5) on arrival to hospital. Nine had been resuscitated from cardiac arrest. There were nine survivors (65%), all with good neurological recovery (Cerebral Performance Category 1–2). Four out of five non-survivors showed cerebral edema already on arrival computed tomographic (CT) scan while none of the nine survivors did.

Conclusions: The results of this study suggest that an early abnormal CT scan of the brain in patients resuscitated after asphyxiation carries an adverse prognosis. The favorable outcome of the patients in the present study suggests that a randomized clinical trial on the use of induced hypothermia in patients exposed to severe asphyxia might be warranted.

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IN 2002, two randomized-controlled trials^{1,2} showed a favorable neurologic outcome and survival with induced hypothermia compared with normothermia in comatose survivors of an out-of-hospital cardiac arrest with ventricular fibrillation as the initial cardiac rhythm. Subsequently, the International Liaison Committee on Resuscitation (ILCOR) recommended that 'unconscious adult patients with spontaneous circulation after out-of-hospital cardiac arrest should be cooled to 32–34 °C for 12–24 h when the initial rhythm was ventricular fibrillation' and that 'such cooling may also be beneficial for other rhythms or in-hospital cardiac arrest'.³

Other causes of cerebral ischemia such as hanging,⁴ drowning⁵ and inhalation of toxic gases^{6–8} carry a very poor prognosis when treated with traditional methods. No controlled clinical trials have been performed in such patients. Animal studies suggest that induced hypothermia can improve neurological outcome after a cardiac arrest following exsanguination^{9,10} and in a randomized-

controlled trial, beneficial effects of moderate hypothermia in perinatal asphyxial encephalopathy have been reported.¹¹ Several case reports on a good neurological outcome using induced hypothermia following hanging^{12–14} and near-drowning¹⁵ have also been published. At our hospital, induced hypothermia has been used for unconscious survivors of a cardiac arrest both in and out of hospital since 2002. Since mid-year 2002, induced hypothermia has also been used in survivors after severe asphyxia due to methane and carbon monoxide intoxication, near-drowning and hanging. The aim of the present study was to report the results of the management of these patients.

Material and methods

The EMS in the greater Reykjavik area is well organized, with well-trained paramedics, and the average response time is 5 min.¹⁶ However, outside

the Reykjavik area, the system is not as well advanced, especially in rural areas. All patients surviving a cardiac arrest or asphyxia in Iceland are referred to Landspítali University Hospital. Since 2002, all comatose survivors of cardiac arrest have been treated with induced hypothermia for 24 h. All survivors of asphyxia after hanging, drowning and other external causes have also been treated in the same way. After approval of the hospital ethics committee and the Icelandic Data Protection Authority, we reviewed the charts of all patients treated with induced hypothermia after asphyxia of external causes in our intensive care units during the period, from 1 July 2002 until 30 June 2009. This included all unconscious patients admitted to the intensive care units after severe asphyxia during this period of time. The criteria used for hypothermia treatment were coma after successful cardiopulmonary resuscitation, evaluated before administration of anesthetic or sedative drugs. In all these cases, patients were intubated and mechanically ventilated at the scene by an emergency team or on arrival to the emergency department at the hospital. On arrival to the hospital emergency department, the Glasgow Coma Score (GCS) was estimated and APACHE II score was recorded after the first 24 h in the intensive care unit. After resuscitation, all the patients were deeply unconscious with a GCS of three to five before sedative drugs were given, but had a stable cardiac rhythm and adequate blood pressure, three with inotropic and/or vasopressor support. After admission to the intensive care unit, the patients were sedated with fentanyl and propofol infusions, mechanically ventilated and induced hypothermia was started. Muscle relaxants were used in some cases to prevent shivering during hypothermia. The target temperature was 32–34 °C using either an external cooling device (Cure Wrap[®], MTRE Advanced Technologies Ltd, Or-Akiva, Israel) or intravascular cooling (CoolGuard 3000[®], Alsium, Irvine, CA). Hypothermia was continued for 24 h, after which the patients were allowed to reach normothermia passively or rewarmed using the intravascular cooling device by changing the set temperature by 0.5 °C/h. Other intensive care treatment was carried out according to the guidelines of our units, such as maintaining the mean arterial pressure above 65 mmHg with the help of intravenous fluids, inotropic and vasopressor agents if necessary. Urine output was maintained above 0.5 ml/kg/h with fluids and diuretics. Lung-protective ventilation was used, with tidal volumes below

6 ml/kg, $\text{FiO}_2 < 0.8$, peak airway pressures below 30 cmH₂O and PEEP 5–15 cmH₂O. Enteral nutrition was started within 24–48 h with the goal of administering 25 kcal/kg/day within 3–4 days. Patients with carbon monoxide intoxication were also treated in a hyperbaric oxygen chamber three times for 2 h at a time during the first 24 h. Cerebral Performance Category (CPC)¹⁷ was used to evaluate the outcome of the patients on discharge. The length of ICU and hospital stay as well as survival were recorded.

Results

Hypothermia was induced in 14 patients following asphyxiation. Five patients died (36%) and the other nine survived with almost full recovery. An overview of all the cases is shown in Table 1, and admission data are shown in Table 2. All patients were male. Intravascular devices were used for cooling in nine cases and external cooling in five cases.

Hypothermia was induced in two patients after suicidal carbon monoxide intoxication. The duration of hypoxia was unknown. They were both comatose but breathing spontaneously and had low oxygen saturation when the emergency team arrived. Both made almost a full recovery, although one of them had minor neurological deficits on discharge (CPC 2).

Induced hypothermia was used in one patient after methane exposure during manure management in a farmhouse. A farmer was found unconscious in a sheep cote having been managing liquid manure. He had last been seen 45 min earlier. Transport time to the hospital was 3 h. On arrival, the patient had spontaneous breathing but he was unconscious with a GCS of 5. The first arterial pH value was 7.26. He stayed 3 days in the ICU and made a full recovery (CPC 1).

Eight patients were treated after suicidal hanging. At the arrival of paramedics, all were unconscious, two were breathing spontaneously and six were in cardiac arrest and received CPR. None of the patients had cervical spine injuries or injuries to major vessels or airways. Three patients died in the hospital, two had an abnormal computed tomographic (CT) scan showing cerebral edema on admission, one was judged to have a normal CT scan on arrival but an MRI 7 days later showed extensive cortical infarction. Five made a full recovery and they all had a normal CT scan on admission. All non-survivors were in cardiac arrest

Table 1

Overview of patients treated after asphyxiation.

Case	Cause of asphyxia	Age	Estimated interval from event to recognition (min)*	Bystander CPR	Clinical condition at scene	Time from recognition to ROSC (min)	GCS	Admission temperature (°C)	ICU stay (days)	Brain imaging	CPC at discharge
1	CO intoxication	24	Unknown	No	SB, Hypoxia	NA	4	38.8	4	MRI normal	1
2	CO intoxication	44	Unknown	No	SB, Hypoxia	NA	5	36.0	4	MRI abnormal	2
3	Methane intoxication	60	<45	No	SB	NA	5	35.6	3	CT normal	1
4	Hanging	24	<30	No	SB	NA	4	36.2	3	CT normal	1
5	Hanging	11	<10	Yes	Cardiac arrest	4	3	37.2	9	MRI and CT normal	1
6	Hanging	19	<7	Yes	Cardiac arrest	20	3	34.2	22	CT normal	5
7	Hanging	37	<5	No	Cardiac arrest seizures SB, hypoxia, seizures	NA	5	36.5	2	MRI abnormal CT normal	1
8	Hanging	32	Unknown	No	Cardiac arrest	Unknown	4	36.4	2	CT normal	1
9	Hanging	24	<30	No	Cardiac arrest	Unknown	3	36.6	7	CT abnormal	5
10	Hanging	21	5	No	Cardiac arrest	10	3	36.7	3	Not performed	1
11	Hanging	44	<20	Yes	Cardiac arrest	12	3	35.0	13	CT abnormal	5
12	Drowning	14	<5	Yes	Cardiac arrest	5	3	35.1	13	CT normal	1
13	Drowning	16	Unknown	Yes	Cardiac arrest	Unknown	3	31.6	22	CT abnormal	5
14	Drowning	9	<15	Yes	Cardiac arrest	7	3	35.2	10	CT abnormal	5

*All events were unwitnessed and therefore length of hypoxia can only be estimated from when the patient was last seen until recognition.

CPR, cardiopulmonary resuscitation; SB, spontaneous breathing; NA, not applicable; ROSC, return of spontaneous circulation; GCS, Glasgow Coma Score; ICU, intensive care unit; CPC, Cerebral Performance Category¹⁷ (1, Good cerebral performance; 2, Moderate cerebral disability; 3, Severe cerebral disability; 4, Coma, vegetative state; 5, Death).

when found but three of the survivors were also in cardiac arrest when found.

Three patients were treated after accidental drowning; all had cardiac arrests. Two of them had a CT scan showing cerebral edema on arrival to the hospital and they both died (CPC 5). One patient had a normal brain CT scan and made a full recovery (CPC 1). The surviving patient was also treated with extra corporal membrane oxygenation (ECMO) for severe respiratory failure due to ARDS.

All patients were deeply comatose (GCS 3–5) after initial resuscitation in the emergency room, but they all had a stable cardiac rhythm and adequate blood pressure (MAP >65 mmHg), three with inotropic and/or vasopressor support. Most of the patients had metabolic acidosis with an

elevation of serum lactate on arrival. Of the nine survivors, CT scan of the brain was performed on arrival in six and was normal in all, two other cases had a normal MRI after a few days and in one case brain imaging was unfortunately not performed. Four out of five non-survivors had an abnormal CT scan already on arrival. In one case, arrival CT was judged normal but an MRI 7 days later showed extensive cortical infarction.

Discussion

The main result of this case series is that nine out of 14 patients, treated with induced hypothermia for severe asphyxia, survived with only minor or no neurological sequelae (CPC 1–2). These results are

Table 2

Admission data.									
Case	Cause of asphyxia	Blood pressure in ER (mmHg)	Heart rate in ER (b.p.m.)	Blood sugar in ER (mmol/l)	Arterial pH	APACHE II	Interval from recognition to start of cooling (h)	Interval from start of cooling to target temp (h)	Cooling method
1	CO intoxication	123/55	146	–	7.51	19	Unknown	11	Intravascular
2	CO intoxication	113/44	89	5.7	6.98	21	8	10	Intravascular
3	Methane intoxication	124/56	113	5.3	7.26	22	3	6.5	External
4	Hanging	95/55	75	4.7	7.29	22	1	5.5	External
5	Hanging	110/60	80	9.3	7.31	17	4	2.5	External
6	Hanging	160/100	135	11.5	7.24	14	1	1	Intravascular
7	Hanging	120/85	82	11.6	7.10	11	2.5	8.5	Intravascular
8	Hanging	150/85	165	6.4	7.38	19	2	19.5	External
9	Hanging	147/55	143	–	7.27	24	1.5	26	External
10	Hanging	120/70	100	6.3	7.27	15	2.5	4	Intravascular
11	Hanging	134/78	120	6.5	–	18	1	1.5	Intravascular
12	Drowning	135/90	100	10.6	7.20	29	2.5	0.5	ECMO
13	Drowning	167/113	107	7.1	–	19	0	0	Intravascular
14	Drowning	110/70	130	10.7	7.22	30	1	4	Intravascular

ER, emergency room; APACHE II, Acute Physiology and Chronic Health Evaluation II²⁶.

in accordance with the current literature. There have been three case reports on induced hypothermia following asphyxia, two after hanging^{12,13} and one after drowning.¹⁵ Recently, a retrospective review on 13 patients was published where induced hypothermia was used following near-hanging.¹⁴ The outcome was good in six out of eight patients not suffering a cardiac arrest and in three out of five suffering a cardiac arrest. At present, no randomized clinical trials are available on this clinical problem.

In our case series, the hypoxic insult was asphyxia and the patients were treated in the same way as comatose patients after a cardiac arrest are treated in our hospital, i.e. according to the recommendations of the ILCOR from 2003.³

In eight of our patients, hanging was the initial insult. Hanging is one of the most common methods of suicide worldwide, with an estimated death rate of 70–80%, and the cause of death is usually asphyxia.¹⁸ Cervical spine injury is relatively rare in suicidal hanging⁴ and none of our patients had cervical spine injuries or injuries to major vessels or airways. The main problem in successfully resuscitated patients is sequelae of hypoxic brain injury. Prognostic factors include hanging time, GCS 3 and especially cardiac arrest when found.¹⁹ In other studies, prognostic factors have included GCS <8, hypotension and an abnormal CT scan of the brain.²⁰ In a review of 42 cases of hanging followed

by a cardiac arrest, there was 100% mortality even when the patients were breathing spontaneously on arrival to hospital.⁴ Among our patients, six out of eight were in cardiac arrest when found and three of them made a full recovery following induced hypothermia while three died. The three patients in our case series admitted after drowning were all in cardiac arrest when found and one of them survived with a full recovery.²¹ The one who survived also had severe respiratory failure, which was treated with ECMO.

If carbon monoxide intoxication leads to unconsciousness, it is believed to be serious and it can cause extensive brain damage.⁶ The two patients in our case series showed signs of severe intoxication but recovered almost fully.

One patient was cooled after being found unconscious during manure management on a farm. Accidents related to manure have been reported and the fatality rate is high.^{7,8} Asphyxiation is the most frequently identified cause of death due to inhalation of manure gas, which is mostly methane and hydrogen sulfide, and this causes hypoxia. One patient in our case series had been unconscious for 3 h on arrival at the hospital after inhalation of manure gas and he recovered fully following induced hypothermia.

Mild induced hypothermia is a relatively safe treatment modality in centers that use it frequently.^{22–25} In our ICU, over 200 patients have

been treated with induced hypothermia after a cardiac arrest and no severe complications connected to the hypothermia treatment have occurred. However, respiratory infections and groin hematomas after catheter insertion do occur occasionally.

In summary, all 14 patients in this case series were deeply comatose (GCS range 3–5) on arrival to the hospital. Nine of them had been resuscitated from a cardiac arrest and most of them had metabolic acidosis on arrival. Following hypothermia treatment 9 out of 14 (64%) survived an asphyxic event and the five patients not suffering cardiac arrest all survived. All of the non-survivors were in cardiac arrest when found, but also four of the survivors. The factor that most strongly correlated with an unfavorable outcome was an abnormal CT scan of the brain on admission to the hospital. None of the survivors had an abnormal brain image but in four out of five non-survivors cerebral edema was evident on arrival CT.

The results of this study suggest that an early abnormal CT scan of the brain in patients resuscitated after asphyxiation carries an unfavorable prognosis. Furthermore, it appears that asphyxia without a cardiac arrest has a better prognosis than asphyxia followed by a cardiac arrest. This study does not provide any proof that therapeutic hypothermia limits the neurologic damage after asphyxiation. But considering the favorable outcome of the patients in the present study compared with the traditional treatment described in the current literature in patients exposed to severe asphyxia, it is suggested that a randomized clinical trial on the use of induced hypothermia is warranted.

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