Pamela Heaberlin, MS, RN, NNP-BC ❍ Section Editor

Monitoring of Pain and Stress in an Infant With Asphyxia During Induced Hypothermia

A Case Report

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ABSTRACT

The purpose of this article was to study an infant who suffered from asphyxia undergoing induced hypothermia with regard to (1) describe the pain and stress as measured by physiological variables skin conductance algesimeter (SCA) and pain rating scales, (2) the correlation between SCA and pain rating scales, and (3) how temperature cycles in the cooling blanket affect the response of the sympathetic nervous system as measured by the SCA and physiological variables. A single prospective case study was used for this article. Data were recorded every 15 minutes for 96 hours. Each observation was categorized according to treatment phase: cooling 0 to 72 hours, rewarming, and controlled normal temperature up to 96 hours. Structured observations were carried out and all nursing care was documented. In addition, 5 periods with no other nursing interventions were identified in which data were recorded every minute for analysis. Skin conductance algimetry showed a variable response during treatment. During cooling, 68% of the 15-minute periods, signs of stress and pain were recorded. During rewarming, the corresponding figure was 83%. During the time sequences with normal temperature, 89% of the periods were associated with stress and pain. During 80% of the nursing procedures, the SCA showed stress and pain. There was no correlation between the pain-rating scales and SCA. When the cooling blanket temperature was lower than core temperature, the infant had more stress and pain according to SCA ($P < .001$) and an increase in heart rate and blood pressure ($P < .001$). In infants during induced hypothermia, SCA seem to detect pain and stress. Future evaluation of SCA for the detection of pain and stress during hypothermia treatment is necessary. Pain-rating scales do not appear reliable in this case report.

Key Words: asphyxia, heart rate variability, induced hypothermia, pain-rating scales, skin conductance algimetry

Asphyxia (from Greek: without a pulse) may occur before, during, or after labor. The reduced oxygen access and the compromised circulation put the infant's internal organs at risk, especially hypoxic-ischemic encephalopathy.[1] The damaging effects of hypoxia can be avoided or reduced by head or whole-body cooling of the infant, known as induced hypothermia.[1,2] It is vital that infants who need cooling treatment are identified and that treatment is started within 6 hours after birth.[3]

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The stress response to hypothermia is different in adults and infants. In adults, hypothermia is counteracted by shivering and vasoconstriction. This response is so vigorous that it has to be canceled out to keep the patient cooled.[4] The infant's muscle mass is too small to counteract the hypothermia, and the vasoconstriction has little effect on reducing heat loss.[5] Instead, infants have a so-called nonshivering thermostat, which includes the activation of noradrenaline and, thyroxine and the metabolism of brown adipose tissue.[5] Adults who are awake during cooling report that shivering is painful and stressful.[6] The question remains how painful/stressful therapeutic hypothermia is for an infant.

Although neonates undoubtedly feel pain and stress, the response to noxious stimuli can be difficult to interpret and cause caregivers to underestimate the infant's distress. Untreated pain can have an untoward effect on the infant's central nervous system development, wound healing, immune function, circulation, and growth.[7] To overcome this problem, pain ration scales are used. They are based on the child's pain signals as expressed through facial expressions, and the signals/movement of the arms, hands, and legs.[7] Pain and stress can also be seen in physiological variables such as heart rate, heart rate variability (HRV), and blood pressure changes.[8,9] Specific pain rating scales to assess infants during hypothermia treatment have not been validated.

Pain and stress-associated sympathetic activation can also be recognized by using a noninvasive method, skin conductance algesimeter (SCA), or electrodermal activity. Skin conductance algimetry measures the emotional stress on the skin and detects nociceptive pain[10] by measuring the changes of electrical conductance caused by activity in the dermal sweat glands.

When the body experiences a threat or pain, the sympathetic nervous system responds to the danger by contracting peripheral blood vessels, increasing blood pressure and heart rate. In humans, sweat glands are most abundant in the palms and soles[11] and SCA is preferentially measured at these locations. The method has been shown to have higher specificity and sensitivity for detecting stress and pain than other available physiological parameters.[10] Skin conductance algimetry has been validated and used in infants[12-15] but has not, to our knowledge, been studied in infants or adults undergoing hypothermia treatment. However, a study has shown that SCA does not react to the ambient temperatures when tested at temperatures between 15° and 45°.[16]

The purpose of this case report of an infant who suffered from asphyxia undergoing induced hypothermia is 3-fold: to describe the pain and stress as measured by physiological variables, SCA, and pain rating scales in response to hypothermia and temperature variations.

MATERIALS AND METHODS

Case History

A full-term infant was born by normal vaginal delivery after an uncomplicated pregnancy, in gestational week 40 +2 in a small district hospital in northern Sweden. The Apgar score was 4, 4, and 4 at 1, 5, and 10 minutes of age, respectively. Although the blood gas from the umbilical cord was normal, the infant deteriorated further, probably because of an occult feto-maternal transfusion and after 30 minutes required advanced cardiopulmonary resuscitation. A blood gas indicated a severe metabolic acidosis with pH < 6.8 and anemia. The infant stabilized and passive cooling started at 1 hour of age. Controlled hypothermia treatment was continued after transfer to the Umeå University Hospital. During transport, the target temperature 33.5°C ± 0.5°C was maintained. At the university hospital, the infant was placed on a servo-controlled cooling blanket (Blanketrol III; Cincinnati Sub-Zero, Cincinnati, Ohio) with a temperature range of 24°C to 42°C. Vital signs, amplitude-integrated electroencephalography (aEEG) (Nicolet ICU monitor; VIASYS Nicolet eeg, Madison, Wisconsin), and fluid balance were carefully monitored. Dopamine was needed to maintain adequate mean blood pressure (>40 mmHg). For sedation, according to a national protocol for neonatal hypothermia, morphine infusion (10 μg/kg per hour) was continuously administrated during treatment. The infant also received phenobarbital because of clinically suspected seizures. After a 72-hour cooling period, the infant's body temperature was increased by 0.5°C per hour to a target temperature of 36.8°C. The infant remained on the cooling blanket for an additional 24 hours after the temperature started to rise to avoid rebound hyperthermia.

Data Collection

Definition of Phases and Sequences During the Collection Period

Overall the observation lasted 96 hours and consisted of 3 phases of controlled induced hypothermia: cooling 0 to 72 hours, rewarming, and controlled normal temperature up to 96 hours. The normal phase was defined as when the infant had reached a target core temperature of 36.8°C and remaining on the cooling blanket. The 96 hours were divided into 15-minute sequences, rendering a total number of 384 time sequences. Each 15-minute sequence was categorized as follows: (*a*) intervention (n = 181) when nursing, medical procedures, physical contact, and the like were performed or (*b*) nonintervention (n = 203). All nursing and medical interventions, physical contacts, and the like, were documented. In addition to these 15-minute

sequences, 5 periods were identified when no nursing interventions occurred (3 during cooling phase, 1 during warming phase, and 1 during normal temperature phase). During these periods, data were analyzed every minute.

Collection of Physiological Variables and Temperatures

The physiological variables measured were heart rate, oxygenation (saturation), blood pressure, HRV, and electrocortical activity by continuous aEEG. Monitoring data were documented every 15 minutes. Heart rate variability was recorded, using a sampling rate of 1000 Hz. The HRV data were divided into 6 sections: (1) average heart rate, (2) total HRV (Ptot), (3) high-frequency HRV, (4) very low frequency (VLF) HRV, (5) low-frequency HRV, and (6) the ratio of low frequency/high frequency. aEEG signals were recorded on a computer with online visualization for the direct observation of seizure activity.

The core body temperature (rectal) and the blanket water temperature ("water temperature") were displayed on the cooling device, registered with a video camera, and stored on an external disc drive. The temperature of the cooling blanket ("blanket temperature") was recorded with a sensor, attached to the surface of the cooling blanket. The temperature measured was divided into 2 categories: cooling and warming. Cooling was defined when the temperature was lower than the infant's core temperature, and warming was defined when the blanket temperature was higher than the infant's core temperature.

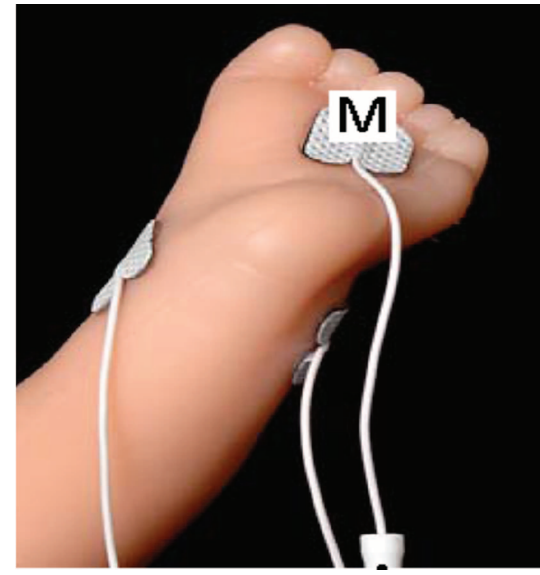
Collection of Skin Conductance

Pain- and stress-associated sympathetic activation was measured by an SCA (Med-Storm Stress Detector, version 1.1; Med-Storm Innovation AS, Oslo, Norway), using its preprogrammed infant measurement setting. To measure the skin conductance in infants, 3 electrodes (reference, current, measuring) are placed on the patient's foot (Figure 1). An example of a recording is shown in Figure 2. Data were processed in a computer program (Med-Storm Application Software) and stored. Skin conductance algimetry responses were divided into 5 categories of pain and stress according to the manufacturer's manual (Table 1).

Assessment of Pain and Behavioral Pattern

Four different pain rating scales for infants and one behavioral scale were used for comparison with SCA. None of these have been validated in infants with hypothermia treatment. The scales were used every half hour and when signs of pain and behavioral pattern changed. The pain scales used were Neonatal Pain Agitation & Sedation Scale, ALPS1, Comfort Neo Scale (Comn), Comfort Behavior Scale (Comb), and behavior scale Prechtl's 5 Point scale.

FIGURE 1.



Placement of the 3 skin conductance algimetry electrodes on the patient's foot. From the user manual of Med-Storm Stress Detector, version 1.1, with permission from the owner, Hanne Storm Med-Storm Innovation AS, Oslo, Norway.

All of these ratings scales are commonly used; they have validity and reliability for neonates.[17-22]

Statistical Analysis

All data were transferred to a spreadsheet and the statistical software program (SPSS 17.0 Advanced Statistical, SPSS, Inc, Armonk, NY). In addition to the descriptive analysis used, the appropriate parametric tests were employed (eg, *t* test, analysis of variance, Pearson correlation) or the appropriate nonparametric tests (Text Mann Whitney *U*, Spearman rank correlation) to detect differences and/or connections. The level of significance of differences was set at $P < .05$.

RESULTS

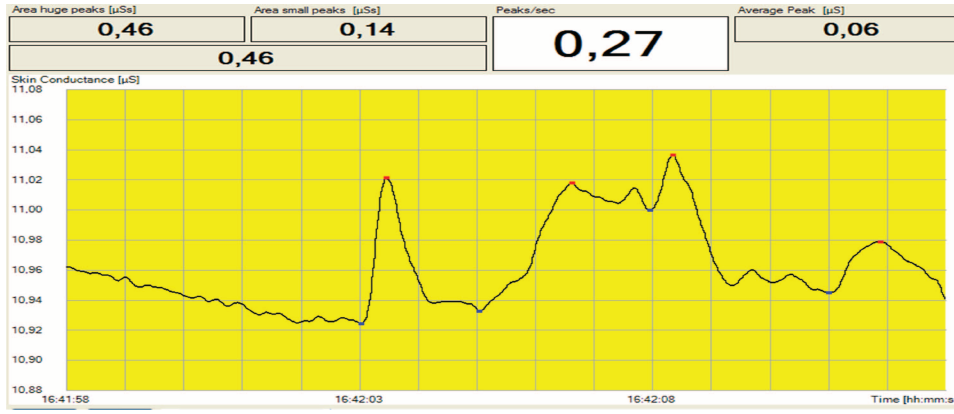
Physiological Variables and Temperatures

During the cooling phase of the induced hypothermia, the core temperature average was 33.5°C (SD = 0.23). The patient's oxygenation during the cooling phase averaged 95% (SD = 3.4) with a mean heart rate of 100 beats per minute (SD = 8.4). The mean blood pressure during cooling was 46 mm Hg (Table 2). Interpretations of the aEEG showed no seizure activity.

SCA During the Different Phases

Throughout all 96 hours, 73% (n = 279) of the 15-minute sequences had a peak on the SCA that

FIGURE 2.



Skin conductance algimetry measures the changes of electrical conductance caused by activity in the dermal sweat glands as a response to pain or stress. The X-axis is time in seconds, here an episode of 15 seconds. The Y-axis represents the skin conductance in micro Siemens (µS). At 16:42:03, an amplitude-integrated electroencephalography needle (used to obtain electrical brain activity) was inserted, resulting in an increase in electrical conductance to approximately 11.02 µS. This is the first peak in this episode and marked with a red dot. The infant wakes up and during fixation of the needle, 3 more peaks are recorded. Altogether, during these 15 seconds, 4 peaks were identified by the software of the equipment, ie, 0.27 peaks per second (shown in the large white box), which is above the threshold value 0.21 peaks per second.

was above the threshold for pain (≥0.21 peaks per second). When the infant was in the cooling phase, there was a peak above the threshold for pain (≥0.21 peaks per second) in 68% (n = 195) of the 15-minute sequences, and in 58% (n = 165) of the periods the peak was above the highest limit (≥0.4 peaks per second) on the SCA. Also, during the warming phase signs of discomfort were obvious with significant peaks in 83% of the 15-minute sequences (Table 3).

During nursing and other physical contact, the SCA showed a peak above 0.21 peaks per second in 80% (n = 85) of the 15-minute sequences. During periods when suction in the endotracheal tube occurred, 82% (n = 35) of the periods had a peak above 0.32 peaks per second. During 37 feeding periods, 74% (n = 27) of the periods peaked above 0.21 peaks per second (Table 4).

Correlations Between SCA, Pain Rating Scales, and the Prechtl Score

No significant correlations were found (Spearman rank correlation) between SCA and pain rating scales during the 15-minute sequences. Where SCA peaked above the highest limit (≥0.4 peaks per second), the pain rating scales did not show evidence of pain in 55% of the periods registered. When the peak on the SCA was just above the threshold for pain (≥0.21 peaks per second), the pain rating scales showed no pain in 65% of the periods. During the warming phase and at normal temperature, there was no indication of pain as determined by the pain scales (Table 5).

The behavior scale, Prechtl's Five Point Scale, showed that the infant had eyes closed in 81% (n = 256) of the 15-minutes sequences, and opened the eyes during 8 of the sequences. In 7 of these, the SCA

TABLE 1. The Skin Conductance Algimetry Manual's Definition of Pain and Stress[a]

Color	Peaks/s	The Infant
White	0.00-0.07	The infant is calm
Light yellow	0.14	The infant is calm and moves a little
Yellow	0.21-0.27	The infant is active, observe the infant, pain/discomfort threshold is reached
Orange	0.33	The infant is probably in pain/discomfort; evaluate the situation
Red	≥0.4	The infant is in increasing pain/discomfort

[a]*When the skin conductance algimetry shows 0.00-0.20 peaks per second, the infant is in no pain, above 0.21 the threshold for pain is reached.*

TABLE 2. Physiological Variables and Temperatures Shown and Divided in All of the 15-Minute Sequences by Intervention and Different Phases of Treatment[a]

Physiological Variable and Temperatures	Sequences	Cooling Phase		Warming Phase		Normal Temperature		96 Hours Total	
		M	SD	M	SD	M	SD	M	SD
Oxygenation	All 15-min sequences	95	3.4	92	3	92	3.9	94	3.6
	Intervention sequences	95	3.5	92	3.3	92	2.5	94	3.6
	Nonintervention sequences	95	3.3	91	2.5	92	2.8	94	3.5
Heart rate	All 15-min sequences	100	8.4	116	12.2	128	9.9	106	14.1
	Intervention sequences	101	8.5	115	14	130	12	106	14.3
	Nonintervention sequences	100	8.3	118	9.5	127	8.3	106	13.9
Mean blood pressure	All 15-min sequences	46	8.6	44	7.2	44	4.1	46	7.9
	Intervention sequences	46	8.9	46	8.8	45	5	46	8.4
	Nonintervention sequ ences	46	8.4	43	4.4	43	3.4	45	7.5
Core temperature	All 15-min sequences	33.5	0.23	35.2	0.82	36.7	0.22	34.2	1.2
	Intervention sequences	33.5	0.25	35	0.91	36.8	0.24	34.1	1.2
	Nonintervention sequences	33.5	0.22	35.5	0.57	36.7	0.21	34.2	1.3
Blanket temperature	All 15-min sequences	30.5	5.5	33.9	6.5	36	4.8	31.7	5.9
	Intervention sequences	30.2	5.3	34.1	6.7	35.6	4.7	31.4	5.7
	Nonintervention sequences	30.8	5.7	33.6	6.4	36.3	4.9	32.1	6
Water temperature	All 15-min sequences	30.5	6.3	33.8	7	36.3	5.4	31.7	6.6
	Intervention sequences	30.3	6	34	6.3	35.8	5.9	31.4	6.4
	Nonintervention sequences	30.7	6.5	33.5	8	36.5	5.2	32	6.7

[a]*Mean (M) and standard deviation (SD) for the physiological variables and temperatures in each phase.*

Table 3. Treatment Phases and Total Treatment Period, by Intervention, and the Highest Peaks Documented During That 15-Min Sequence. (n = Number of 15-Min Sequences)

Phase and Sequences Type	Max Peaks/s, % (n)					
	0.00-0.13 % (n)	0.14-0.20 % (n)	0.21-0.32 % (n)	0.33-0.39 % (n)	≥ 0.4 % (n)	Total % (n)
Intervention sequences						
Cooling phase	16 (22)	7 (10)	5 (6)	7 (10)	65 (90)	
Warming phase	0 (0)	12 (2)	6 (1)	6 (1)	76 (13)	
Normal temperature	4 (1)	7 (2)	0 (0)	4 (1)	85 (22)	
Total intervention sequences	12 (23)	8 (14)	4 (7)	7 (12)	69 (125)	100 (181)
Nonintervention periods						
Cooling phase	35 (53)	5 (8)	6 (9)	3 (5)	50 (75)	
Warming phase	15 (2)	8 (1)	8 (1)	15 (2)	54 (6)	
Normal temperature	5 (2)	5 (2)	3 (1)	3 (1)	85 (34)	
Total nonintervention sequences	28 (57)	5 (11)	5 (11)	4 (8)	57 (116)	100 (203)
Whole 96-hour period						
Cooling phase	26 (75)	6 (18)	5 (15)	5 (15)	58 (165)	
Warming phase	7 (2)	10 (3)	7 (2)	10 (3)	66 (20)	
Normal temperature	10 (3)	6 (4)	1 (1)	7 (2)	85 (56)	
Total 96-hour period	20 (80)	7 (25)	5 (18)	5 (20)	63 (241)	100 (384)

TABLE 4. Percentage and Frequency of the Number of Maximum Peak/s Skin Conductance Algimetry Measurements by 2 Different Nursing Interventions and 3 Treatment Phases (n = Number of 15-min Sequences)

	Maximum Peaks/s				
Nursing Intervention	**0.00-0.13**	**0.14-0.20**	**0.21-0.32**	**0.33-0.39**	**≥0.4**
Endotracheal tube suction					
Cooling phase	22% (n = 6)	7% (n = 2)	0% (n = 0)	14% (n = 4)	57% (n = 16)
Warming phase	0% (n = 0)	0% (n = 0)	0% (n = 0)	20% (n = 1)	80% (n = 4)
Normal temperature	0% (n = 0)	0% (n = 0)	0% (n = 0)	20% (n = 1)	80% (n = 9)
Total	13% (n = 6)	5% (n = 2)	0% (n = 0)	14% (n = 6)	68% (n = 29)
Feeding					
Cooling phase	19% (n = 5)	8% (n = 2)	8% (n = 2)	12% (n = 3)	54% (n = 14)
Warming phase	0% (n = 0)	0% (n = 0)	0% (n = 0)	0% (n = 0)	100% (n = 2)
Normal temperature	11% (n = 1)	22% (n = 2)	0% (n = 0)	0% (n = 0)	67% (n = 6)
Total	16% (n = 6)	11% (n = 4)	5% (n = 2)	8% (n = 3)	60% (n = 22)

had a peak higher than the highest limit (≥0.4 peaks per second). When the patient opened the eyes and moved at some time during 4 out of the 15 minutes periods, the SCA response showed a high level of discomfort. During the observation, the infant was never seen crying (Table 6).

Effect of Temperature Cycles in the Cooling Blanket on SCA and Physiological Variables

Figure 3 shows the relationship between the cooling blanket temperature fluctuations, the infant's body temperature, and the peaks from SCA during the 5 different minute data periods. When the cooling blanket's temperature was lower than the core temperature, the infant had more pain and stress, according to SCA as compared to when the blanket was warming ($P < .001$).

When the blanket's temperature was lower than body temperature, a significant increase in heart rate and mean blood pressure occurred ($P < .001$). The SCA highest peaks per second were also significantly higher when the blanket was cooling than when it was warming ($P < .001$). No significant changes in HRV were found (Table 7).

DISCUSSION

Skin conductance algimetry has been reported for more than 10 years to be a measure of discomfort caused by pain and stress in infants regardless of environmental temperature, cardiorespiratory status, or neuromuscular blockade, and has been claimed to detect nociceptive pain better than other objective methods.[10,23,24] Studies in adults who communicated the level of discomfort showed a direct significant correlation between SCA and pain.[25-27]

More recent studies confirm that SCA detects pain in both preterm and term infants and further indicate the differentiation of pain and discomfort.[28,29] However, to our knowledge, no study of pain assessment using SCA in infants undergoing treatment with hypothermia has yet been preformed. In this case report, throughout all 15-minute sequences during treatment with hypothermia, outbreaks of pain and stress were frequently present according to SCA with an increase in stress/pain levels when the blanket was cooling and also during the warming phase. Furthermore, SCA also indicated increased stress and pain during nursing interventions.

Physiological signs of pain such as heart rate, blood pressure, oxygen saturation, and HRV are also often used to identify pain in infants.[30] These physiological signs seem to be short and go unnoticed, or its variations can be influenced by the hypothermia treatment making assessment of physiological signs over prolonged period of time more difficult. In this case report, the average heart rate and mean arterial pressure were higher, while oxygenation was lower when the blanket was cooling as compared with warming. This might indicate that cooling is more stressful. On the contrary, HRV was inconclusive and may be difficult to interpret during hypothermia.

Various validated pain assessment tools based on behavioral signs have been reported,[31,32] but none of these have been validated for infants undergoing hypothermia treatment. It is important to remember that there are no validated pain scales in infants during hypothermia treatment, but they are still used in this patient group. In this case report, no correlations

TABLE 5. Number of 15-Min Sequences With a Maximum Peak/s in the Corresponding Interval (0-0.013, 0.14-0.20, 0.21-0.32, 0.33-0.39, and ≥0.4) for Each Pain Rating Scale Comparison of Pain Rating and Skin Conductance Algimetry During the Hypothermia Treatment Phases by Situations With No Pain vs Pain, With the Maximum Peak on the Skin Conductance Algimetry

			Maximum Peaks/s				
Phase	**Rating Scale**	**Pain or No Pain**	**0-0.013**	**0.14-0.20**	**0.21-0.32**	**0.33-0.39**	**≥0.4**
Cooling phase	N-pass	No pain	61	14	12	14	138
		Pain	0	1	0	0	7
	Comfort BS	No pain	61	13	12	13	131
		Pain	0	2	0	1	14
	Comfort NS	No pain	61	13	11	13	128
		Pain	0	2	1	1	17
	ALPS 1	No pain	60	13	12	12	111
		Pain	1	2	0	2	34
Warming phase	N-pass	No pain	2	3	2	3	20
		Pain	0	0	0	0	0
	Comfort BS	No pain	2	3	2	3	20
		Pain	0	0	0	0	0
	Comfort NS	No pain	2	3	2	3	20
		Pain	0	0	0	0	0
	ALPS 1	No pain	2	3	2	3	20
		Pain	0	0	0	0	0
Normal temperature	N-pass	No pain	3	4	1	1	28
		Pain	0	0	0	0	0
	Comfort BS	No pain	3	4	1	1	28
		Pain	0	0	0	0	0
	Comfort NS	No pain	3	4	1	1	28
		Pain	0	0	0	0	0
	ALPS 1	No pain	3	4	1	1	28
		Pain	0	0	0	0	0
Total	N-pass	No pain	66	21	15	18	186
		Pain	0	1	0	0	7
	Comfort BS	No pain	66	20	15	17	179
		Pain	0	2	0	1	14
	Comfort NS	No pain	66	20	14	17	176
		Pain	0	2	1	1	17
	ALPS 1	No pain	65	20	15	16	159
		Pain	1	2	0	2	34

Abbreviations: ALPS, Astrid Lindgren Children's Hospital Pain Scale; BS, Comfort Behavior Scale; NS, Comfort Neo Scale.

between commonly used pain rating scales and other physiological signs of pain could be found. This supports the experience by others who have questioned the benefit of pain rating scale in these patients.[33] The Prechtl scale showed that the infant had no established signs of pain during treatment, and thereby also indicating the problem with behavior scales for assessment of discomfort.

In an animal study, plasma cortisol levels during hypothermia were increased during the hypothermia phase and almost tripled during warming, as compared with the animals kept at normal temperature.[34] This

TABLE 6. Prechtl Score and Skin Conductance Algimetry: Percentage and Number of 15-Minute Sequences with a Maximum Peak/s in the Corresponding Interval (0-0.013, 0.14-0.20, 0.21-0.32, 0.33-0.39, and ≥0.4) Divided Into Each Prechtl Score[a]

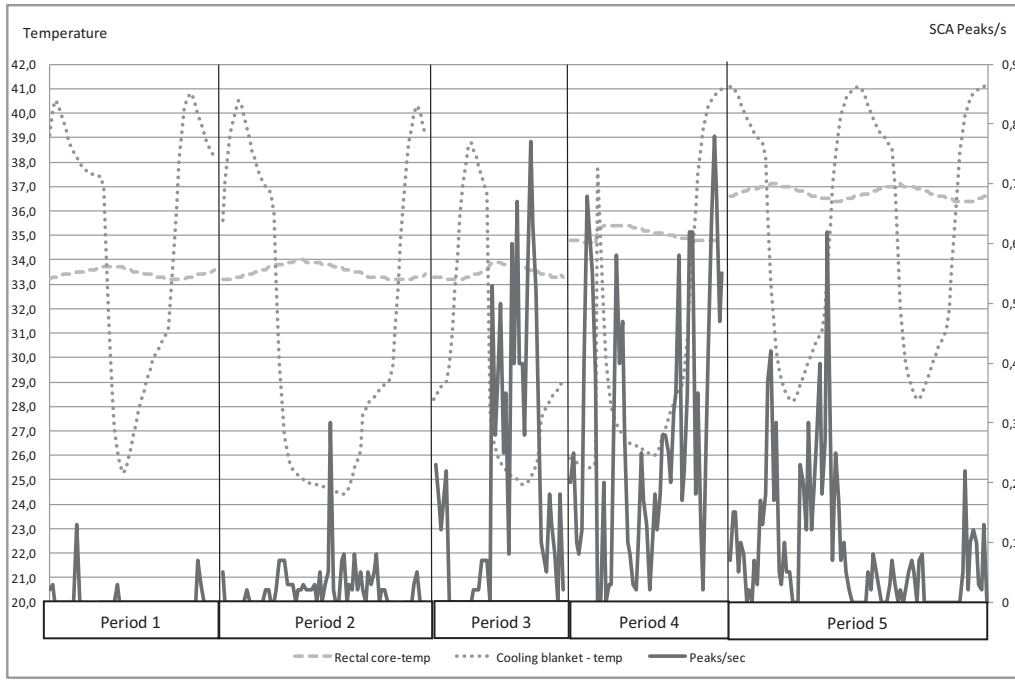
Prechtl Score		Maximum Peaks/s				
		0.00-0.13	0.14-0.20	0.21-0.32	0.33-0.39	≥0.4
1p	Eyes closed, regular respiration, no movements	20% (n = 61)	6% (n = 20)	4% (n = 13)	4% (n = 14)	47% (n = 148)
2p	Eyes closed, irregular respiration, small movements	1% (n = 3)	1% (n = 3)	0.3% (n = 1)	1% (n = 3)	12% (n = 36)
3p	Eyes open, no movements			0.3% (n = 1)		2% (n = 7)
4p	Eyes open, gross movements				0.3% (n = 1)	1% (n = 3)
5p	Crying (vocalization)					

[a]*Prechtl score showing the patient's movements and maximum peak of the skin conductance algimetry response (n = times of rating during a 15-minute sequences).*

pattern may also have been reflected in the SCA response of the infant with the most pronounced response during the rewarming cycle.

The infant had periods with high number of peaks per second recorded by the SCA when caregivers preformed rather harmless nursing interventions, for example, only touching. It has been reported that sick term infants in the NICU had a higher stress response with a higher median baseline salivary cortisol level compared with healthy infants, and

FIGURE 3.



The relationship between the cooling blanket temperature fluctuations, core temperature, and peaks per second from skin conductance algimetry during the 5 different minute data periods.

TABLE 7. Changes in Physiological Variables Relative to the Blanket Cooling or Warming

Physiological Variable	Blanket Activity	n	*M*	SD	*P*
Oxygenation	Cooling	196	93	3.0	$P < .001$
	Warming	144	94	3.7	
Heart rate	Cooling	195	110	15.5	$P < .001$
	Warming	144	103	12.0	
Average blood pressure	Cooling	196	44	6.1	$P < .001$
	Warming	144	41	6.7	
SCA peaks/s	Cooling	196	0.31	0.3	$P < .001$
	Warming	139	0.14	0.2	
HRV total	Cooling	83	3.17	0.5	NS
	Warming	56	3.28	0.6	
HRV VLF	Cooling	83	2.39	0.5	NS
	Warming	56	2.4	0.6	
HRV LF	Cooling	83	2.84	0.6	NS
	Warming	56	2.96	0.6	
HRV HF	Cooling	74	2.42	0.6	NS
	Warming	56	2.54	0.7	
HRV ratio VLF/LF	Cooling	74	0.44	0.3	NS
	Warming	56	0.42	0.3	

Abbreviations: HF, high frequency; HRV, heart rate variability; LF, low frequency; NS, not significant; SCA, skin conductance algimetry; VLF, very low frequency.

were also more stressed during procedures that should not be painful, like nappy change.[35] This suggests that sick infant in the NICU, also those treated with hypothermia, are under stress and may be hypersensitive to touching and pain. Continuous SCA monitoring during hypothermia warrants further evaluation as a new tool where physiological signs and rating scales for evaluation of discomfort seem to be inherent.

Animal studies have showed that adequate sedation is essential for optimal neuroprotection and stress reduction.[34] It is reasonable to think that asphyctic infants react in a similar way. In therapeutic hypothermia for adults, analgesia with opioids is standard care.[36,37] We believe that adequate sedation and analgesia should also be standard of care in infants undergoing hypothermia treatment. Results from this case study suggest that SCA can be an interesting tool to identify discomfort in infants treated with hypothermia and to evaluate the effects of analgesia.

References

1. Volpe JJ. *Neurology of the New Born*. 5th ed. Philadelphia, PA: Sanders Elsevier; 2008.
2. Shah PS, Ohlsson A, Perlman M. Hypothermia to treat neonatal hypoxic ischemic encephalopathy: systematic review. *Arch Pediatr Adolesc Med*. 2007;161:951-958.
3. Thoresen M. Hypothermia after perinatal asphyxia: selection for treatment and cooling protocol. *J Pediatr*. 2011;158:45-49.
4. Daniel I, Sessler M. Thermoregulatory defense mechanisms. *Crit Care Med*. 2009;37:203-210.
5. Boxwell G, ed. *Neonatal Intensive Care Nursing*. London, England: Routledge; 2001.
6. Kammersgaard L, Rasmussen B, Jørgensen H, Reith J, Weber U, Olsen T. Feasibility and safety of inducing modest hypothermia in awake patients with acute stroke through surface cooling: a case-control study: the Copenhagen Stroke Study. *Stroke*. 2000;31:2251-2256.
7. Gradin M, Larsson BA, Lindh V, Selander B, Norman E. Nationella riktlinjer för prevention och behandling av smärta i nyföddhetsperioden. http://www.svenskbarnsmartforening.se/svenskbarnsmartforening/dokument/nyfoddhetssmarta.pdf. Published 2009. Accessed November 9, 2009.
8. Okan F, Ozdil A, Bulbul A, Yapici Z, Nuhoglu A. Analgesic effects of skin-to-skin contact and breastfeeding in procedural pain in healthy term neonates. *Ann Trop Paediatr*. 2010;30:119-128.
9. Gjerstad A, Wagner K, Henrichsen T, Storm H. Skin conductance versus the modified COMFORT sedation score as a measure of discomfort in artificially ventilated children. *Pediatrics*. 2008;122:848-853.
10. Storm H. Changes in skin conductance as a tool to monitor nociceptive stimulation and pain. *Curr Opin Anaesthesiol*. 2008;21:796-804.
11. Sonesson B, Sonesson G. *Anatomi och fysiologi*. Falköping, Sweden: Elanders Gummesons; 2001.
12. Cresi1 F, Castagno E, Storm H, Silvestro L, Miniero R, Savino F. Combined esophageal intraluminal impedance, pH and skin conductance monitoring to detect discomfort in GERD infants. *PLoS ONE*. 2012;7:e43476.
13. Eriksson M, Storm H, Fremming A, Schollin J. Skin conductance compared to a combined behavioural and physiological pain measure in newborn infants. *Acta Pædiatr*. 2008;97:27-30.
14. De Jesus A, Tristao R, Storm H, da Rocha A, Campos D Jr. Heart rate, oxygen saturation, and skin conductance: a comparison study of acute pain in Brazilian newborns. *Conf Proc IEEE Eng Med Biol Soc*. 2011:1875-1879.
15. Ham J, Tronick E. A procedure for the measurement of infant skin conductance and its initial validation using clap induced startle. *Dev Psychobiol*. 2008;50:626-631.
16. Bini G, Hagbarth KE, Hynninen P, Wallin BG. Thermoregulatory and rhythm-generating mechanisms governing the sudomotor and

vasoconstrictor outflow in human cutaneous nerves. *J Physiol*. 1980; 306:537-552.
17. Neonatal Pain, Agitation & Sedation Scale. http://www.n-pass.com/assessment_guidlines.html. Published 2004. Accessed October 22, 2010.
18. Riktlinjer för smärtbehandling vid Astrid Lindgrens barnsjukhus. http://www.karolinska.se/upload/Astrid%20Lindgrens%20Barnsjukhus/Barnanestesi%20och%20intensivv%C3%A5rd/Sm%C3%A4rtbehandlingsenheten/Riktlinjer20110201.pdf. Published 2011. Accessed March 13, 2013
19. van Dijk M, Roofthooft D, Anand K, et al. Taking up the challenge of measuring prolonged pain in (premature) neonates: the COMFORTneo scale seems promising. *Clin J Pain*. 2009;25:607-616.
20. van Dijk M, Peters J, van Deventer P, Tibboel D. The COMFORT Behavior Scale: a tool for assessing pain and sedation in infants. *Am J Nurs*. 2005;105:33-36.
21. Hummel P, Puchalski M, Creech S, Weiss M. Clinical reliability and validity of the N-PASS: neonatal pain, agitation and sedation scale with prolonged pain. *J Perinatol*. 2008;28:55-60.
22. van Dijk M, de Boer J, Koot H, Tibboel D, Passchier J, Duivenvoorden H. The reliability and validity of the COMFORT scale as a postoperative pain instrument in 0 to 3-year-old infants. *Pain*. 2000;84:367-377.
23. Storm H. Skin conductance and the stress response from heel stick in preterm infants. *Arch Dis Child Fetal Neonatal Ed*. 2000;83:143-147.
24. Hellerud BC, Storm H. Skin conductance and behaviour during sensory stimulation of preterm and term infants. *Early Hum Dev*. 2002;70:35-46.
25. Reinhardt T, Schmahl C, Wüst S, Bohus M. Salivary cortisol, heart rate, electrodermal activity and subjective stress responses to the Mannheim Multicomponent Stress Test (MMST). *Psychiatry Res*. 2012;198:106-111.
26. Ledowski1 T, Bromilow J, Paech MJ, Storm H, Hacking R, Schug SA. Monitoring of skin conductance to assess postoperative pain intensity. *Br J Anaesth*. 2006;97:862-865.
27. Storm H, Shafiei M, Myre K, Raeder J. Palmar skin conductance compared to a developed stress score and to noxious and awakening stimuli on patients in anaesthesia. *Acta Anaesthesiol Scand*. 2005;49:798-803.
28. Pereira-da-Silva L, Virella D, Monteiro I, et al. Skin conductance indices discriminate nociceptive responses to acute stimuli from different heel prick procedures in infants. *J Matern Fetal Neonatal Med*. 2012;25:796-801.
29. Munsters J, Wallström L, Agren J, Norsted T, Sindelar R. Skin conductance measurements as pain assessment in newborn infants born at 22-27 weeks gestational age at different postnatal age. *Early Hum Dev*. 2012;88:21-26.
30. Raeside L. Physiological measures of assessing infant pain: a literature review. *Br J Nurs*. 2011;20:1370-1376.
31. Duhn LJ, Medves JM. A systematic integrative review of infant pain assessment tools. *Adv Neonatal Care*. 2004;4:126-140.
32. Hummel P, van Dijk M. Pain assessment: current status and challenges. *Semin Fetal Neonatal Med*. 2006;11:237-245.
33. Chirinian N, Mann N. Therapeutic hypothermia for management of neonatal asphyxia: what nurses need to know. *Critical Care Nurse*. 2011;31:1-12.
34. Thoresen M, Satas S, Løberg EM, et al. Twenty-four hours of mild hypothermia in unsedated newborn pigs starting after a severe global hypoxic-ischemic insult is not neuroprotective. *Pediatr Res*. 2001;50:405-411.
35. Mörelius E, Hellström-Westas L, Carlén C, Norman E, Nelson N. Is a nappy change stressful to neonates? *Early Hum Dev*. 2006;82: 669-676.
36. Zobel C, Adler C, Kranz A, et al. Mild therapeutic hypothermia in cardiogenic shock syndrome. *Crit Care Med*. 2012;40:1715-1723.
37. Weant KA, Baker SN. Pharmacologic management during therapeutic hypothermia. *Adv Emerg Nurs J*. 2011;33:288-296.