The gradient between the central and skin temperature as an early marker in the detection of blood-culture-proven neonatal sepsis;

A retrospective, observational cohort study

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INTRODUCTION

Neonatal sepsis is one of the most severe conditions in neonates admitted to the Neonatal Intensive Care Unit (NICU), especially in neonates with a very low birth weight (<1500 grams) (1-4). Approximately 20% of neonates admitted to the NICU develop sepsis (5). Neonatal sepsis may lead to serious complications, like bronchopulmonary dysplasia, patent ductus arteriosus, neurodevelopmental impairment and even death (2). Roughly 50% of neonatal mortality is caused by sepsis (6). Initial signs and symptoms of neonatal sepsis are subtle and non-specific. Suspicion of sepsis is based on clinical symptoms and positive laboratory parameters (7). Symptoms include: apneic attacks; lethargy; peripheral circulation; bradycardia; tachycardia; hypotension; respiratory distress; poor skin colour; irritability; feeding problems; abdominal distension; prolonged jaundice; fever and temperature instability (8). The main laboratory findings consist of an increased C-reactive protein (CRP) (≥10 mg/l) and thrombocytopenia (<150*10^3/L) (8,9). The gold standard for diagnosing sepsis is based on a positive blood culture (BC) obtained after neonates are suspected of sepsis (1). A positive BC results in the diagnosis blood-culture-proven sepsis, a negative BC in non-proven sepsis.

Neonatal sepsis is divided into two subtypes, depending on the onset when the first symptoms occur. Early Onset Sepsis (EOS) presents within the first 72 hours of life, while Late Onset Sepsis (LOS) occurs after 72 hours of life (2). Mortality rates due to EOS and LOS are respectively about 13% and 19.7% (6). EOS is often caused by vertical transmission of bacteria from mothers to neonates during childbirth and is frequently associated with obstetric complications, such as premature onset of labour, chorioamnionitis, premature rupture of membranes and peripartum maternal fever (10). LOS is mostly due to hospital-acquired microorganisms (2,5) and often horizontal transmitted via invasive or direct contact with healthcare workers (5,11). Neonates admitted to the NICU are at high risk for LOS due to their undeveloped immune system, long-term need for central venous access, and prolonged hospitalization (2). This study focuses primarily on LOS.

To prevent complications and neonatal death caused by blood-culture-proven sepsis, it is important to promptly start antibiotic treatment after obtaining a BC. Therefore, early diagnosis of blood-culture-proven sepsis is needed. Nurses working at the NICU have an important role in dealing with sepsis. They are the first line of defence in preventing infections, recognizing symptoms of sepsis, reporting related concerns to the physicians and advocating that the neonate receive a timely diagnostic sepsis workup and empiric antibiotic treatment (12). However, recognizing blood-culture-proven sepsis is often difficult because

presenting symptoms may clinically not be distinguished from neonates without an infection (3,11,13,14). If blood-culture-proven sepsis can be diagnosed in an earlier stage, antibiotic treatment can be started earlier. This might result in better survival chances and less complications.

Therefore, the development of sepsis-specific markers is essential. In case of an infection, peripheral vasoconstriction is a common physical reaction in neonates. The peripheral temperature decreases and the basal temperature increases to fight against the infection (15). It is therefore hypothesised that the gradient between the central and skin temperature (temperature gradient) can be a useful marker in the detection of neonatal sepsis. This is supported by several studies, which have shown that an increase of the temperature gradient with 2.0-3.5°C is suggestive for neonatal sepsis (1,14,16,17). However, none of these studies made distinction between blood-culture-proven and non-proven sepsis. Furthermore, the influence of antibiotics on the temperature gradient is not yet determined. Antibiotics treat the bacterial infection, it is therefore hypothesised that the temperature gradient will normalize after starting antibiotic treatment.

Problem statement

Blood-culture-proven sepsis is a common cause of neonatal death, therefore early detection of sepsis is needed to promptly start antibiotic treatment. Since nurses working at the NICU have a crucial role in observing and recognizing early symptoms of neonatal sepsis and temperature measurement is a safe and simple tool to detect blood-culture-proven sepsis, it is important to examine if the temperature gradient can be used as an early marker in the detection of blood-culture-proven sepsis. This is endorsed in several studies, however these studies made no distinction between blood-culture-proven and non-proven sepsis. Therefore, this study will examine the association between the temperature gradient and the early detection of blood-culture-proven sepsis in neonates admitted to the NICU. In addition, the influence of antibiotic treatment on the temperature gradient will be examined.

Objective

The objective of this study is to examine the association of the gradient between the central and skin temperature and the early detection of blood-culture-proven sepsis in neonates admitted to the NICU. This enables nurses working at the NICU to detect blood-culture-proven sepsis in an earlier stage.

Research questions

1. What is the association of the gradient between the central and skin temperature and the early detection of blood-culture-proven sepsis in neonates admitted to the Neonatal Intensive Care Unit?

2. What is the influence of antibiotic treatment, started after a blood culture was obtained, on the gradient between the central and skin temperature?

METHODS

Study design and setting

A retrospective, observational cohort study was conducted at a Dutch NICU. Data was used from neonates admitted to the NICU between January 2012 and December 2013. A retrospective design was chosen in order to achieve the required sample size within the period of this study. A cohort was chosen to avoid selection bias based on the outcome of the study or values of the dependent variables. In order to determine the association between the temperature gradient and blood-culture-proven sepsis distinction between groups was made on the outcome of the BC, positive or negative. Temperature gradients were determined at three time points (figure 1). The first two time points were measured in order to test if the temperature gradient can be used as an early marker for blood-culture-proven sepsis. These time points were 24 (with a range of 36-12) hours prior to the obtained BC (T0) and the moment the BC was obtained (T1), with a range of 12 hours prior to and six hours after the BC was obtained. A third time point, 24 (with a range of 12-36 hours) hours after the BC was obtained (T2), was measured in order to test for effects over time within and between the groups and to determine the influence of antibiotic treatment on the temperature gradient.

(Figure 1)

Participants

All neonates admitted to the NICU between January 2012 and December 2013 were eligible for this study when they were suspected of sepsis and a BC was obtained. Furthermore the central and skin temperatures were measured at all three time points. Exclusion criteria were: neonates with therapeutic hypothermia; consultation of the clinical geneticist, because of suspected genetic disorders what possibly results in an abnormal temperature regulation; a BC obtained at birth, because of premature birth instead of suspected sepsis; no informed consent of the parents/guardians. The initial obtained positive BC of each neonate was used in this study. In absence of a positive BC, the first negative BC was used.

A list of neonates admitted to the NICU between January 2012 and December 2013, with one or more obtained BC's, was received from the laboratory of the NICU under study. All records of these patients were searched in the Patient Data Management System (PDMS) and assessed for the in- and exclusion criteria. Data was manually extracted from the patient records.

Variables

Demographic and clinical data was gathered as baseline information to assess differences between both groups, in order to detect the presence of confounders and for the generalizability of the results. Dichotomous data included gender, presence of central venous lines (CVL), antibiotic treatment, mortality rate, thrombocytopenia and an increased CRP. Continuous data included gestational age (GA), birth weight (BW) and postnatal age. APGAR-score and bacterial pathogens, in case of a positive BC, were included as ordinal data.

The dependent variable in this study was the outcome of the BC: positive (blood-culture-proven sepsis) or negative (non-proven sepsis). The independent variables were the temperature gradients measured at T0, T1 and T2. Temperature gradients were calculated by taking the absolute difference between the central and the skin temperature in Celsius degrees (°C). The rectal temperature was preferably used as central temperature, but in absence of the rectal temperature, the axillary temperature was used. Both temperatures were measured with the same validated digital thermometers with an accuracy of 0.1°C. The skin temperature was continuously measured using a validated sensor placed in the diaper of the neonates. Nurses processed and validated all temperature values in PDMS.

Statistical methods

Statistical tests were performed using SPSS for MAC, version 19.0. All statistical tests were two-sided, significance was defined as $p < 0.05$. Normality of the data was assumed, since $n > 30$ (18).

Clinical and demographic characteristics

Groups were compared on clinical and demographic data using independent sample T-test (continuous data); Chi-square test (dichotomous data) and Mann-Whitney U test (ordinal data). Data that differed between groups and were related to the outcomes of the study were included to the statistical tests as covariates to control for confounding. These include five covariates: BW, GA and presence of a CVL, because a low BW or GA and presence of a CVL are independent risk factors for sepsis (19); thrombocytopenia, because this is a predictor for sepsis (9,19); antibiotic treatment, because antibiotics treat the infection and could therefore have influenced the temperature gradients measured at T2.

Association of the temperature gradient with blood-culture-proven sepsis

The association of the temperature gradients and the detection of blood-culture-proven sepsis was explored by multivariate logistic regression, using a forward LR model (inclusion

a=0.05; exclusion a=0.10). Odds ratios (OR) and 95% confidence intervals (CI) were calculated. An OR>1 suggests a positive association with sepsis and is therefore a possible risk factor whereas an OR<1 suggests a negative association with sepsis and is therefore a possible protective factor. An OR=1 suggests no association (20). Multivariate logistic regression model was generated with the outcome of the BC being the dependent variable and the temperature gradients measured at T0 and T1 being the independent variables. T2 was excluded as independent variable, since at this time point neonates were already suspected of sepsis and could therefore not be used as an early marker for sepsis. The covariate antibiotic treatment was excluded from the model, since antibiotic treatment started after obtaining a BC and could therefore not had any influence on the temperature gradients measured at T0 and T1.

Two subgroup analyses based on BW and GA were performed, since a low BW and GA are independent risk factors for sepsis (19). Subgroup 1 consisted of neonates with a BW ≤1500 gram or GA ≤30 weeks; in subgroup 2 these parameters were respectively ≤1000 grams and ≤26 weeks. The subgroup analyses only contained the covariates "thrombocytopenia" and "presence of a CVL", since the subgroups already adjusted for GA and BW.

Effect over time

ANOVA for repeated measures was used to test for effects over time within and between both groups and to test the influence of antibiotic treatment, started after T1. Temperature gradients measured at T0, T1 and T2 (figure 1) were included in the model as time factors.
To conduct an ANOVA for repeated measures, the assumptions of sphericity and equality of variances must be met. This was evaluated using Mauchly's Test of Sphericity and Levene's Test (20).

Sample size

Sample size for logistic regression was calculated following the guideline of Hosmer and Lemeshow (20). This guideline indicated that the minimum number of cases per independent variable equals ten. For logistic regression two independent variables and four covariates were used. This resulted in a required sample size of at least 60 neonates per group in the first analysis. The subgroup analyses contained two independent variables and two covariates. Therefore, a sample size of at least 40 neonates per group was required.

Consent and ethical approval

The study protocol was approved by the scientific commission of Division Women and Baby of the NICU under study and by the Research Ethics Committee, who gave a non-WMO

statement, protocol number 14-039/C. Parents/guardians were presumed to consent to the use of their child's data for the purposes of scientific research, unless they opt out. All parents/guardians were informed via a patient information dossier when their child was admitted to the NICU. Objection was listed in PDMS.

RESULTS

Clinical and demographic characteristics

(Figure 2)

From January 2012 until December 2013, 668 neonates were eligible for this study. Of these, 504 neonates were excluded. Reasons for exclusion were genetic disorders (17%); therapeutic hypothermia (6%); BC obtained at birth (64%) and missing temperature values (13%). A total of 164 neonates were included in this study: 78 neonates with blood-culture-proven sepsis and 86 with non-proven sepsis (figure 2). Subgroup 1 consisted of 65 neonates with blood-culture-proven sepsis and 68 neonates with non-proven sepsis, in subgroup 2 these numbers were respectively 37 and 48.

(Table 1)

As shown in table 1, blood-culture-proven sepsis was often caused by the bacterial pathogen coagulase negative staphylococcus (65.4%) and staphylococcus aureus (10.2%). In one case, a fungus (candida) caused sepsis. Demographic and clinical characteristics are summarized in table 2. BW, GA, antibiotic treatment, presence of a CVL and thrombocytopenia were variables that significant differ between both groups.

(Table 2)

Variables associated with blood-culture-proven sepsis

Results from multivariate logistic regression (table 3) showed that GA was negative associated with blood-culture-proven sepsis, OR=0.489. The presence of a CVL was positive associated with blood-culture-proven, OR=2.284. In both subgroups only the presence of a CVL was positive associated with blood-culture-proven sepsis, whereas neonates with a BW ≤1500 grams or GA ≤30 weeks had an OR of 2.596 and neonates with a BW ≤1000 grams or GA ≤26 weeks had an OR of 4.792.

Variables not associated with blood-culture-proven sepsis

Temperature gradients measured at T0 and T1 (figure 2) and the covariates BW and thrombocytopenia were not significantly associated with blood-culture-proven sepsis and were therefore excluded from the logistic regression model (table 3). Subgroup analyses also found no significant association between the temperature gradients measured at T0 and T1 and blood-culture-proven sepsis.

(Table 3)

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Effect over time

ANOVA for repeated measures was used to test for effects over time. Levene's Test indicated that assumption of homogeneity of variances had been violated, since one level of the repeated measures variables was significant, p=0.004. Therefore data was transformed using squared root, this resulted in p-values >0.05 in all levels of the repeated measures variables. Mauchly's Test of Sphericity indicated that the assumption of sphericity had not been violated, $X^2(2)$=0.546, p=0.761

Tests of within-subject and between-subject effects showed that, after controlling for the effect of GA, BW, presence of a CVL, thrombocytopenia and antibiotic treatment, there were no significant differences of the temperature gradients within (p=0.708) and between (p=0.305) the blood-culture-proven sepsis and non-proven sepsis groups (table 4).
(Table 4)

DISCUSSION

The findings of this study demonstrated that temperature gradients measured at T0 and T1 were not significant associated with blood-culture-proven sepsis. Subgroup analyses based on BW and GA did not change these results. Repeated measures for ANOVA found no significant differences of the temperature gradients measured at T0, T1 and T2 within and between both groups. This confirms the obtained results from logistic regression and indicates that antibiotic treatment had no influence on the temperature gradients.

The present results contradict earlier studies that reported significant associations between temperature gradients and sepsis, caused by peripheral vasoconstriction (1,14,17,21). This might be explained by the location the skin temperature was measured. In this study the temperature sensor was placed in the diaper, whereas other studies placed the sensor at the sole (1,14,17,21). It is assumed that temperatures measured at extremities are lower than abdominal temperatures, because of reduced blood flow in these areas (22,23). Furthermore, Blackburn e.a. (2001) concluded that lying on the temperature sensor resulted in higher temperature values by comparing temperature sensor placements at the back and abdomen (23). It is therefore plausible that a sensor placed in the diaper will result in higher temperature values compared with a sensor placed at the sole, due to the close position to neonate's basal system and the increased likelihood that neonates lay on the sensor. Probably therefore, the temperature gradient in this study did not increase in neonates with blood-culture-proven sepsis and is probably no predicting value for blood-culture-proven sepsis.

A secondary explanation for the contradicting results could be the fact that this study compared neonates with blood-culture-proven sepsis with neonates with non-proven sepsis, whereas other studies compared septic neonates (both blood-culture-proven and non-proven) with non-sepsis suspected neonates (14,17,21). This study revealed the same temperature gradient profile in both the blood-culture-proven and non-proven sepsis groups, omitting a control group with non-sepsis suspected neonates might explain the contradicting results. Since this study focused on the association between the temperature gradient and blood-culture-proven sepsis only a distinction between neonates with blood-culture-proven sepsis and neonates with non-proven was made. Addition of a non-sepsis control group had therefore no clear added value.

Strengths and limitations

Several strengths and limitations were present. Strengths consist of the ratio between blood-culture-proven sepsis and non-proven sepsis groups. Both group sizes were almost comparable and had enough power to test for a significant association. Furthermore, the same digital thermometers and temperature sensors were used, which benefits the validity of the study results. Eventually, this is probably the first study that investigated the association of the temperature gradient with blood-culture-proven sepsis, whereas other studies made no distinction between blood-culture-proven and non-proven sepsis.

Limitations consist of possible occurrences of measurement bias. Primarily, in the NICU under study nurses must manually validate the skin temperature hourly. However, this was not practised in all cases, in addition nurses validated unlikely low temperatures probably due to an incorrect placement of the temperature sensor in the diaper. Exclusion of these values was determined on the basis of clinical knowledge of the researcher. However, the researcher was not present at the moment of measurement and was not aware of the prevailing circumstances. Therefore, this could have led to biased results.

Secondary, in this study the central temperature was measured either rectal or axillar. It is discussible whether these methods are interchangeable for all neonates admitted to the NICU. Studies showed that axillary temperatures were significant lower compared with rectal temperatures in neonates, except in premature neonates, due to the high permeability of their skin (24,25). This implies that axillar temperatures were only interchangeable with rectal temperatures in premature neonates and could have led to measurement bias. However, subgroup analysis did not found a significant association between the temperature gradient and blood-culture-proven sepsis in neonates with a BW $\leq$1500 grams or GA $\leq$30 weeks, this subgroup included 81,1% of all enrolled neonates. Furthermore, only 40 temperature measurements were axillary compared with 428 rectal measurements. Therefore the risk for bias, due to the method of measuring the central temperature, was small.

Results may be generalizable to other NICU's if in- and exclusion criteria are taken into account as well as the methods of measuring the central and skin temperatures.

Clinical relevance

This study revealed that, in case the skin temperature is measured in the diaper, nurses working at the NICU could not use the temperature gradient as an early marker of blood-culture-proven sepsis. Nevertheless, measuring both the central and skin temperature remains an important task for nurses as well as the early detection of neonatal sepsis.

Several studies revealed that fluctuations of the central temperature are useful in the detection of neonatal sepsis (3,21), where premature septic neonates often suffer from hypothermia and term septic neonates from hyperthermia (3,17,21,26). In the NICU under study the skin temperature, measured in the diaper, is used as an indicator of the central temperature. With regard to the detection of neonatal sepsis, it is therefore important to keep measuring both the skin and central temperature. More research is needed to determine if the skin temperature measured at the sole, instead of a sensor placed in the diaper, can be useful as an early marker in the detection of blood-culture-proven sepsis.

CONCLUSION AND RECOMMENDATIONS

Conclusion

If the skin temperature is measured with a sensor placed in the diaper, the gradient between the central and skin temperature cannot be used as an early single marker in the detection of blood-culture-proven neonatal sepsis, even after adjusting for GA and BW. Antibiotic treatment also has no effect on the temperature gradients in neonates with blood-culture-proven sepsis compared with neonates with non-proven sepsis.

Recommendations

Further research is required in order to confirm the results of this study. Since the location at which the temperature sensor is placed may have influenced the results, it is recommended to perform a study that makes distinction between a sensor to measure the skin temperature placed in the diaper and placed at the sole. This is possible by setting up a multi-centre study, in which each centre will be randomized for measuring the skin temperature with a sensor placed in the diaper or at the sole. Furthermore, addition of a non-sepsis suspected neonatal control group is recommended, in order to determine if neonatal sepsis (both blood-culture-proven and non-proven) can be detectable in an earlier stage using the temperature gradients.

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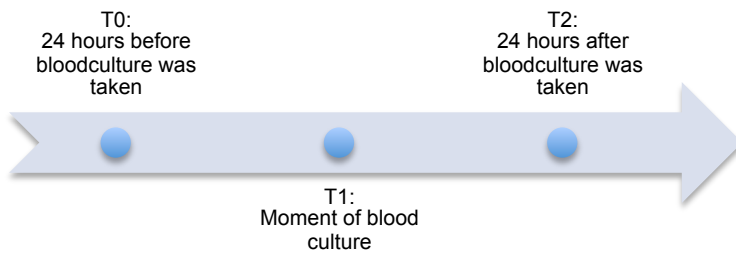
FIGURES AND TABLES

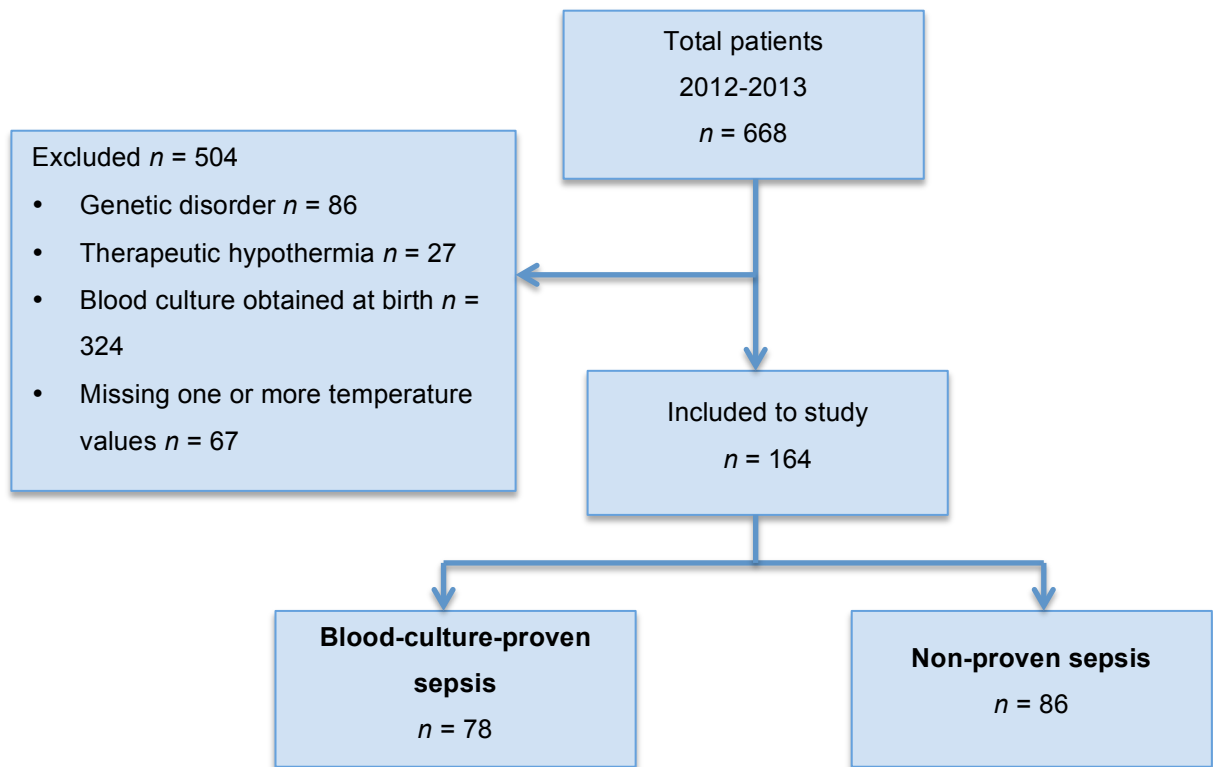Figure 1: Timeline of measuring the gradients between the central and skin temperature

Figure 2: Flowchart of the inclusion process

Table 1: Bacterial pathogens isolated from blood cultures

Name of the isolate	Frequency	%
Coagulase negative staphylococcus	51	65.4
Staphylococcus aureus	8	10.2
Enterobacter	4	5.1
Escherichia	4	5.1
Enterococcus	4	5.1
Serratia	2	2.6
Bacillus	2	2.6
Pseudomonas	1	1.3
Granulicatella	1	1.3
Candida (fungus)	1	1.3

Table 2: Demographic and clinical characteristics

	Blood-culture proven sepsis	Non-proven sepsis	P-value
Gender (Male/Female) [1]	41 / 37	46 / 40	0.906
Postnatal age at onset of suspected sepsis, (mean, range) [2]	13 (2 - 88)	10 (1-113)	0.145
Gestational age, weeks (mean, range) [2]	28.0 (23.9 - 39.3)	30.0 (24.0 - 40.1)	0.000
Birthweight, grams (mean, range) [2]	1045 (485 - 3410)	1376 (605 - 3960)	0.001
APGAR score, 1 minute (median, range) [3]	6 (2 - 10)	6 (0 - 9)	0.716
APGAR score, 5 minutes (median, range) [3]	8 (3-10)	8 (0-10)	0.899
Antibiotic use (%) [1]	100	90.7	0.006
Central Venous Line (%) [1]	39.7	20.9	0.009
Mortality rate during admission (%) [1]	10.3	5.8	0.293
Thrombocytopenia < 150*10^3/L (%) [1]	45.5	25.0	0.006
C-Reactive Proteïn ≥ 10mg/L (%) [1]	63.6	53.6	0.196

[1] Chi-square test
[2] Independent t-test
[3] Mann-Whitney U-test

Table 3: Results from multivariable logistic regression analyses

		Variables included in the logistic regression model					Variables excluded from the logistic regression model		
		Regression coëfficiënt	Odds Ratio	Lower	Upper	P-value		Score	P-value
All included neonates	Constant	4,439	84,722			0,002	Gradient between the central and skin temperature at T0(°C)	2	0,198
	Central Venous Line	0,826	2,284	1,103	4,729	0,026	Gradient between the central and skin temperature at T1 (°C)	0,379	0,538
	Gestational age	-0,164	0,849	0,771	0,934	0,001	Trombocytes <150*10^3/L	3,493	0,062
							Birth weight (grams)	0,194	0,66
Subgroup 1 Neonates BW ≤1500 grams or GA ≤30 weeks	Constant	-0,223	0,8			0,293	Gradient between the central and skin temperature at T0 (°C)	1	0,454
	Central Venous Line	0,954	2,596	1,188	5,672	0,017	Gradient between the central and skin temperature at T1 (°C)	0,82	0,365
							Trombocytes <150*10^3/L	3,743	0,053
Subgroup 2 Neonates BW ≤1000 grams or GA ≤26 weeks	Constant	-0,223	0,8			0,415	Gradient between the central and skin temperature at T0(°C)	1	0,251
	Central Venous Line	1,567	4,792	1,682	13,646	0,003	Gradient between the central and skin temperature at T1 (°C)	0,819	0,365
							Trombocytes <150x10^3/L	0,825	0,364

BW = Birth weight

GA = Gestational age

Table 4: Effects over time within and between subjects

Within-subjects			Between-subjects		
	F	Significance		F	Significance
Intercept	5.885	0.016	Time factor	1.063	0.347
Gestational age (weeks)	0.409	0.523	Time * Gestational age (weeks)	0.487	0.615
Birth weight (grams)	2.647	0.106	Time * Birth weight (grams)	0.168	0.845
Presence of Central Venous Line	0.351	0.554	Time * Presence of Central Venous Line	0.521	0.595
Antibiotic use	1.044	0.309	Time * Antibiotic use	1.412	0.245
Time * Presence of thrombocytopenia ($<150*10^3$/L)	0.036	0.849	Time * Presence of thrombocytopenia ($<150*10^3$/L)	1.098	0.335
Effect groups (blood-culture proven sepsis and non-proven sepsis)	1.060	0.305	Time * Groups (blood-culture proven sepsis and non-proven sepsis)	0.345	0.708

SAMENVATTING

Titel: De gradiënt tussen de centrale temperatuur en huidtemperatuur als vroege marker voor de detectie van bloedkweek bewezen neonatale sepsis; een retrospectieve observationele cohort studie.

Achtergrond: Sepsis is een belangrijk probleem bij neonaten opgenomen op de Neonatale Intensive Care Unit (NICU). Het klinisch beeld van bewezen sepsis begint vaak met niet-specifieke symptomen, maar kan snel verergeren. Vroege diagnose van bewezen sepsis is belangrijk om tijdig antibioticumbehandeling te kunnen starten en de kans op complicaties en mortaliteit te reduceren. Een vergroting van de gradiënt tussen de centrale temperatuur en huidtemperatuur (deltatemperatuur) is een mogelijke indicator voor de vroege detectie van bewezen sepsis.

Doel en onderzoeksvragen: Associatie tussen de deltatemperatuur en de vroege detectie van bewezen sepsis bij neonaten opgenomen op de NICU onderzoeken, met als doel om bewezen sepsis in een eerder stadium te kunnen detecteren. Onderzoeksvragen: "Wat is de associatie tussen de deltatemperatuur en de vroege detectie van bloedkweek bewezen sepsis bij neonaten opgenomen op de NICU?" en "Wat is de invloed van antibioticum, gestart na afname van de bloedkweek, op de deltatemperatuur?"

Methode: Neonaten opgenomen op de NICU tussen januari 2012 en december 2013 kwamen in aanmerking voor de studie indien zij verdacht werden van sepsis en er een bloedkweek was afgenomen. De associatie tussen de deltatemperatuur en de detectie van bewezen sepsis is onderzocht met multivariate logistische regressie. ANOVA voor herhaalde metingen is gebruikt om effecten over de tijd en de invloed van antibioticum te testen.

Resultaten: Achtenzeventig neonaten met bewezen sepsis en 86 neonaten met niet-bewezen sepsis zijn geïncludeerd. Er zijn geen significante associaties tussen de deltatemperatuur en bewezen sepsis gevonden in logistische regressie. ANOVA voor herhaalde metingen liet geen significante verschillen binnen en tussen de groepen zien.

Conclusie: De deltatemperatuur kan niet gebruikt worden als vroege marker voor de detectie van bewezen sepsis. Tevens heeft antibioticumbehandeling geen invloed op de deltatemperatuur.

Aanbevelingen: Multi-centrum studie die onderscheid maakt tussen de plaatsen waarop de huidtemperatuur wordt gemeten en tevens een controlegroep toevoegt met neonaten die niet verdacht worden van sepsis.

Trefwoorden: Neonatale sepsis – Temperatuur – Antibioticum behandeling – Neonatologie – Detectie

ABSTRACT

Title: The gradient between the central and skin temperature as an early marker in the detection of blood-culture-proven neonatal sepsis; a retrospective observational cohort study.

Background: Sepsis is a major problem in neonates admitted to the Neonatal Intensive Care Unit (NICU). Clinical presentation of blood-culture-proven sepsis often starts with nonspecific symptoms, but can quickly deteriorate. Early diagnosis of blood-culture-proven sepsis is important to promptly start antibiotic treatment and to reduce the risk of complications and mortality. An increase of the gradient between the central and skin temperature (temperature gradient) can be a useful marker for the early detection of blood-culture-proven sepsis.

Aim and research questions: To examine the association of the temperature gradient and the detection of blood-culture-proven sepsis in neonates admitted to the NICU, aiming to detect blood-culture-proven sepsis in an earlier stage. Questions: "What is the association of the temperature gradient and the early detection of blood-culture-proven sepsis in neonates admitted to the NICU?" and "What is the influence of antibiotic treatment, started after a blood culture was obtained, on the temperature gradient?"

Method: Neonates admitted to the NICU between January 2012 and December 2013 were eligible for this study when they were suspected of sepsis and a blood culture was obtained. Association between the temperature gradients and the detection of blood-culture-proven sepsis was explored by multivariate logistic regression. ANOVA for repeated measures was used to test for effects over time and to test the influence of antibiotic treatment.

Results: Seventy-eight neonates with blood-culture-proven sepsis and 86 with non-proven sepsis were included in the study. No significant associations between temperature gradients and blood-culture-proven sepsis were found in logistic regression. ANOVA for repeated measures indicated no significant differences within and between both groups over time.

Conclusion: The temperature gradient cannot be used as an early marker in the detection of blood-culture-proven sepsis. Additionally, antibiotic treatment has no influence on the temperature gradient.

Recommendations: Multi-centre study that distinguishes the location at which the skin temperature is measured and adds a non-sepsis suspected neonatal control group.

Keywords: Neonatal sepsis – Temperature – Antibiotic treatment – Neonatology - Detection