

Skin conductance as a marker of pain in infants of different gestational age

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Aims. To assess the use of skin conductance as an objective measure of pain in infants of different gestational age. A second aim was to investigate the relationship between skin conductivity and selected physiological and behavioural variables (oxygen saturation, heart rate and behavioural state).

Methods. Infants were divided according to gestational age into the following 3 groups; group A: 25+0 – 31+6 weeks (13 infants), group B: 32+0 – 35+6 weeks (25 infants), group C: 36+0 – 41+6 weeks (19 infants). The pain stimulus was blood sampling.

Results. The most sensitive parameter for describing changes in skin conductance related to pain was peak per second. No other parameter correlated with the physiological variables chosen. The results showed that the inability to determine basal skin conductance is a crucial disadvantage to practical application. The lack of correlation between conductance parameters and gestational age is surprising.

Conclusion. We conclude that the Peak per Second is the best parameter for evaluating skin conductance in infants and it is not influenced by gestational age. Peaks per Second correlate only with Prechtl's Scale of behavioural state and not with the physiological parameters chosen.

Key words: electrical skin conductivity, gestational age, infants, pain, behavioural state

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INTRODUCTION

The International Association of Study of Pain – IASP defines pain as „unpleasant sensorial or emotional experience which is associated with immediate or potential damage of tissue“. Although more than 40 scoring schemes and pain evaluation scales have been published in the last two decades¹⁻³ the IASP, as an international authority, recommend only the following scales: 1) Neonatal Infant Pain Scale and Premature Infant Pain Profile (PIPP) for evaluation of acute procedural pain, 2) Crying, Required O₂, Increased Vital Signs, Expression, Sleeplessness for evaluation of postoperative pain, 3) Echelle Douleur Incomfort Nouveau-Né for evaluation of permanent, persisting or continuing pain. However, the problem with these scoring schemes apart from PIPP is that they do not distinguish infant gestational age⁴.

Measurement of changes in electrical skin conductivity (SC) appears to be a suitable method for measurement and evaluation of pain in infants as it eliminates the above problems of scoring schemes^{5,6}. The basis of this method is the reactions of the sympathetic nervous system^{7,8}. This is induced by painful stimuli which activate a cascade of physiological reactions resulting in sweat gland activity on the palmar side of the hand and plantar side of the foot^{9,10}. Increase in electrical SC in these areas can be measured⁵. Decrease in skin resistance up to the moment of sweat reabsorption is a manifestation^{8,9} mea-

surable as a conductivity maximum (peak). Changes in electrical SC take place almost immediately in response to painful stimulus, in about 0.7 to 2 sec after impulse¹¹. Measurement of electrical SC is an accepted method for assessing the new-born emotional state and is closely related to infant behaviour and crying¹², which is reflected in the behavioural state of the infant according to Prechtl's method for the qualitative assessment of general movements (Prechtl's Scale) (ref.^{13,14}).

The aim of this study was to determine if changes in electrical SC can be considered an objective method for measurement and assessment of pain in infants of different gestational age. A second aim was to compare these changes with changes in selected physiological parameters during painful stimulus.

MATERIALS AND METHODS

We used the Med-Storm skin conductivity algometer (Med-Storm Inovation, Norway) to determine SC. The “preterm” mode which is a specific setting for infants was used. The system is able to measure conductivity in the range 1 to 200 μ S with a noise level maintained below 0.002 μ S. The algometer is able to record any deviation or error of measurement, such as poor contact of electrodes, as well as any interference with other electrical devices. The following parameters – Peaks per Second

(PpS) and Area under Curve (AUC), which consist of Area Small Peaks (ASP) and Area Huge Peaks were measured. Standardly, three AgCl self-adhesive electrodes denoted as follows are employed: C - current, R - reference and M - measurement. These are placed on an area of the infant's foot, where maximum density of sweat glands can be found. The area under the M - the electrode is decisive for measurement as its electrical SC value reflects the amount and activity of sweat glands.

Experimental

We focused on infants from an intensive care unit, intermediary care and infants from rooming-in at the Neonatological Department of Tomas Bata Regional Hospital in Zlín, the Czech Republic. The informed consent of parents was obligatory for participation. The physiological parameters heart rate (HR) and oxygen saturation (SatO₂) were also measured. Of contextual parameters we decided to study gestational age and Prechtl's Scale of behavioural state. The infants were divided according to gestational age (GA) as follows: group A (GA-A):25+0 - 31+6 weeks (13 infants), group B (GA-B): 32+0 - 35+6 weeks (25 infants) and group C (GA-C):36+0 - 41+6 weeks (19 infants).

According to Prechtl's Scale, infants were separated into 5 categories^{13,14}. To prevent distortion of results we included only infants who met the criteria for categories 1 and 2. Response of the neonate to painful stimuli is significantly influenced by the state of consciousness and behaviour (sleep, wakefulness, restlessness).

Capillary blood sampling was used as the painful stimulus. Postnatal age does not play any major role in this but measurement in the case of immature infants was carried out once they had stable blood pressure and circulation. Infants whose clinical condition or therapy could affect the results of objective measurements for example worsening clinical status, increasing body temperature, decreasing O₂ saturation, etc., were excluded as were infants on artificial ventilation. Feet were cleaned by normal physiological saline and the electrodes were then attached. A saturation sensor was then attached.

The experiment was divided into three phases - pre-stimular, stimular and post-stimular phase. In each phase, electrical SC, SatO₂, HR were measured. During the **pre-stimular phase**, parameters of electrical SC were recorded for 2 min. Changes in categorization of Prechtl's scale were also recorded for each infant. Sucrose solution (25%) in a volume 0.1 - 0.5 mL was administered to the patient at the end of this phase for about 2 min before blood sampling (i.e. painful stimulus). Infants received a volume of 0.1 mL to 1 kg of body weight, 0.2 mL to 2 kg, 0.3 mL to 3 kg, 0.4 mL to 4 kg and 0.5 mL above 4 kg weight. This dosage was applied on a dummy to follow the pain prevention protocol standardly used at the Neonatological department in Tomas Bata Regional Hospital in Zlín. In the second phase, the **stimular phase** the painful stimulus was capillary blood sampling. Recording of changes in electrical SC using Med-Storm algemeter began simultaneously with the painful stimulus. SatO₂ and HR were measured in accordance with blood sampling. The as-

essment of Prechtl's Scale was done at the beginning and at the end of the stimular phase. All measurements were completed 1 min after the end of blood sampling. After termination of painful stimulus, we waited for the infants to calm down, which lasted an average of 3 - 5 min. Through the **Post-stimular phase** skin conductivity changes and others parameters were recorded for one minute.

Statistical analysis

Although measurement of variables was performed for a longer period, the data from the first 15 s were used for statistical evaluation. Outlying data were excluded using the Q test. Tables, basic statistical parameters and Spearman correlation coefficients were done in STATISTICA software. The Mixed Linear Model was used to determine the impact of parameters on the ASP and PpS using SAS for Windows, version 9.1.2. Gestational age and interaction between phases of our test and Prechtl's Scale values were included as fixed factors into the model.

RESULTS

As can be seen from Table 1, there was no significant relation between gestational age and electrical SC values - ASP and PpS. Gestational age is thus not an important factor in the assessment of pain in infants using skin conductance.

The second aim was to investigate any relationship between skin conductivity changes, presented as parameters ASP and PpS, and selected physiological and contextual parameters (Table 2). The results showed no significant relationship between the values of HR, SatO₂, Prechtl's Scale and electrical SC parameters. A significant correlation was found only between ASP and PpS in all phases. Significant correlations between contextual parameter presented by Prechtl's Scale and SC parameters (ASP and PpS) were found in the post-stimulation phase only. Similar results are shown by the correlations for differences in values of parameters in different phases of the test (Table 3). From these results it is obvious that both APS and PpS have comparable validity. However, PpS has greater statistical significance which shows that PpS is a sufficient parameter for pain assessment.

Although this correlation shows the PpS is a better parameter for pain evaluation because there were more significant differences between PpS in different phases and behavioural state than ASP (Table 4). In addition we compared the SC parameters and behavioural state in individual phases of the test - before, during and after painful stimulus. As can be seen, the results show high variability of ASP values in the infants. A significant difference was found only between the pre-stimular phase with Prechtl 2 and post-stimular phase with Prechtl 1. All results unexpectedly showed low validity of the ASP indicator wrt phase of the test and behavioural state. PpS had slightly higher validity than ASP. Here the high statistical significance was in values of PpS between pre-stimular phase and the present value of Prechtl 1 and Prechtl 2 and

next among pre-stimular phase with Prechtl 1 and painful phase with Prechtl 3. Therefore it is probably better to evaluate pain γ using this parameter of SC. As the results show it is impossible to specify the basal skin conductivity in these short times. Continuous recording of SC in an individual infant has greater informational value and it is possible to evaluate pain via increasing frequency of peaks per second.

DISCUSSION

There are a number of publications on pain perception in infants e.g. Storm et al.⁹ who studied the dependence of electrical SC on painful stimuli in 20 preterm infants (29 - 35 day of gestational ages). They established that during painful stimulus the frequency of PpS increases while no PpS before or after painful stimulus was detected. This corresponds to the results of the present study as well as to another study by Storm et al. In a study published in 2008 (ref.¹⁵) they were unable to establish the basal line SC. They only described an increase in basal line dur-

ing painful stimulus which persisted in the post-stimular phase. Harrison et al. came to the same conclusions¹⁶. Another study showing variability in skin conductivity changes¹⁷, compared skin conductivity changes with behaviour of both preterm and full term infants. The influence of both nociceptive and tactile stimulation on SC changes is described. Their results also confirm an increase in SC during nociceptive stimulus.

Perception of painful stimuli is developed in both preterm and full term infants very well. However, term infants are not used to dealing with painful stimuli. Their behaviour is just more organized^{18,19}. Much work has been done relating to pain assessment in preterm infants. However there is currently no reliable, valid and objective physiological measure of pain in infants.

Table 1 describes how gestational age affects response to painful stimuli, ASP and PpS parameters as well. Mean values of ASP and PpS parameters across groups A to C do not differ significantly, indicating that these parameters do not depend on gestational age. Storm⁹ focused on dependence between parameters of gestational age and number of peaks observed as well as their amplitude. Our

Table 1. ASP and PpS according to gestational age (LSM \pm SD).

Gestational age	ASP	PpS
31+6 - 25+0 (GA-A)	0.2160 \pm 0.2352	0.3117 \pm 0.0835
35+6 - 32+0 (GA-B)	0.5512 \pm 0.2151	0.3583 \pm 0.0707
41+6 - 36+0 (GA-C)	0.5310 \pm 0.1982	0.4378 \pm 0.0705

GA-A, B, C - gestational age, group A, B, C; ASP - Area Small Peaks; PpS - Peak per Second

Table 2. Spearman correlation coefficient for differences in values of studied parameters within individual phases of the test.

	SatO ₂	HR	Prechtl	ASP	PpS
Pre-stimular Phase 1					
SatO ₂	1.00	-0.10	-0.20	0.09	0.02
HR	-0.10	1.00	-0.02	-0.06	-0.09
Prechtl	-0.20	-0.02	1.00	0.08	0.02
ASP	0.09	-0.06	0.08	1.00	0.68*
PpS	0.02	-0.09	0.02	0.68*	1.00
Stimular Phase 2					
SatO ₂	1.00	-0.13	-0.12	-0.13	-0.04
HR	-0.13	1.00	0.13	-0.22	-0.15
Prechtl	-0.12	0.13	1.00	0.25	0.13
ASP	-0.13	-0.22	0.25	1.00	0.75*
PpS	-0.04	-0.15	0.13	0.75*	1.00
Post-stimular Phase 3					
SatO ₂	1.00	0.08	-0.26	-0.15	-0.10
HR	0.08	1.00	0.14	-0.05	0.02
Prechtl	-0.26	0.14	1.00	0.39*	0.37*
ASP	-0.15	-0.05	0.39*	1.00	0.90*
PpS	-0.10	0.02	0.37*	0.90*	1.00

Marked correlation are significant on level of provability $P < 0.05$

SatO₂ - oxygen saturation; HR - heart rate; Prechtl - Prechtl's Scale; ASP - Area Small Peaks; PpS - Peak per Second

Table 3. Spearman correlation coefficient for differences in values of studied parameters between individual phases of the test.

	SatO ₂ 2-1	HR 2-1	Prechtl 2-1	ASP 2-1	PpS 2-1
SatO ₂ 2-1	1.00	0.19	0.08	-0.23	-0.33*
HR 2-1	0.19	1.00	0.07	-0.14	-0.07
Prechtl 2-1	0.08	0.07	1.00	0.12	0.16
ASP 2-1	-0.23	-0.14	0.12	1.00	0.51*
PpS 2-1	-0.33*	-0.07	0.16	0.51*	1.00
	SatO ₂ 2-3	HR 2-3	Prechtl 2-3	ASP 2-3	PpS 2-3
SatO ₂ 2-3	1.00	0.00	0.05	-0.16	-0.13
HR 2-3	0.00	1.00	0.08	-0.01	-0.24
Prechtl 2-3	0.05	0.08	1.00	0.17	0.08
ASP 2-3	-0.16	-0.01	0.17	1.00	0.46*
PpS 2-3	-0.13	-0.24	0.08	0.46*	1.00
	SatO ₂ 1-3	HR 1-3	Prechtl 1-3	ASP 1-3	PpS 1-3
SatO ₂ 1-3	1.00	0.15	-0.21	0.05	-0.17
HR 1-3	0.15	1.00	-0.06	-0.22	-0.26
Prechtl 1-3	-0.21	-0.06	1.00	0.13	0.26
ASP 1-3	0.05	-0.22	0.13	1.00	0.62*
PpS 1-3	-0.17	-0.26	0.26	0.62*	1.00

Marked correlation are significant on level of provability $P < 0.05$

Described correlation (2-1; 2-3; 1-3) mean difference of the measured value in different phases of the test. SatO₂ – oxygen saturation; HR - heart rate; Prechtl – Prechtl's Scale; ASP – Area Small Peaks; PpS – Peak per Second

Table 4. ASP a PpS according to phase and Prechtl's Scale (LSM ± SD).

Phase	Prechtl	ASP	PpS
Pre-stimular	1	0.6786 ± 0.2478	0.2907 ± 0.07409*
Pre-stimular	2	0.8158 ± 0.2101*	0.4502 ± 0.06343**a
Pre-stimular	3	0.04172 ± 1.1382	0.5429 ± 0.3315
Stimular	1	0.07337 ± 0.8026	0.2915 ± 0.2355
Stimular	2	0.3877 ± 0.2531	0.4058 ± 0.07520a
Stimular	3	0.7359 ± 0.3143	0.5401 ± 0.09342**a
Stimular	4	0.9417 ± 0.3303	0.4228 ± 0.09646a
Stimular	5	0.2627 ± 0.5083	0.4605 ± 0.1489a
Post-stimular	1	0.3050 ± 0.2230**	0.1877 ± 0.06729b
Post-stimular	2	0.5950 ± 0.2309	0.3903 ± 0.06953 a
Post-stimular	3	0.06923 ± 0.8020	0.1155 ± 0.2349

Different indexes in columns determine statistically provable differences $P < 0.1$ (*, **); $P < 0.05$ (a,b)

stud shows no significant correlation between gestational age and PpS during painful stimulus, just as gestational age affects neither level of basal line of electrical SC nor behavioural state of an infant during painful stimulus.

A comparison of SC parameters with selected physiological parameters was studied by Roeggen et al. in Australia in 2011 (ref.²⁰). Our results (Tables 2 and 3) showed that there were no correlation between physiological parameters and SC parameters. Moreover, no correlation, either in shift of skin conductivity parameters between individual phases (Table 2) or between phases themselves (Table 3), was found. The only statistically significant correlation can be established between ASP and PpS values but not in relation to physiological parameters. Mutual correlation between ASP and PpS was 0.51 in phase 2-1 and 0.46 in phase 2-3 and 0.62 in phase 1-3. Statistically significant was a negative correlation between

SatO₂ and PpS parameters -0.33 $P = 0.05$, but only in shift between phases 2 and 1 (Table 3).

For individual phases of the test, which are described in Table 2, statistically significant correlation was found again only between parameters of SC. Correlation between ASP and PpS was 0.68 in the pre-stimular phase, 0.75 in the stimular phase and 0.90 in the post-stimular phase 3. In addition there was a statistically significant correlation between parameters of SC and values of Prechtl behavioural state in the post-stimular phase. There was a statistically significant correlation between parameters PpS and Prechtl of 0.37 and between ASP and Prechtl of 0.39. Storm claims that the behavioural state of an infant reflects the number of PpS during painful stimulus⁹.

CONCLUSION

This study deals with objectification of painful stimulus evaluation in infants, in particular with relationship between skin conductivity and selected physiological parameters in different gestational categories. The results show it is necessary to focus on individual assessment during evaluation of pain in infants, as there is no universal basal level of skin conductivity. It is highly specific for given infant. We confirm the previous studies which show that only real Peaks per second have high validity for pain assessment in all gestational categories. Skin conductivity is not significantly influenced by either the phase of the test or the gestational age of infant. Likewise, it is impossible to determine basal lines of electrical skin conductivity. Data are valid only for a given individual infant. Skin conductivity changes are most probably influenced by many others factors, not exclusively by painful stimuli. However this method can assist pain assessment in infants, which due to its complexity requires a wide choice of techniques. No relationship between physiological parameters and parameters of SC was confirmed.

As a limitation of this study can be considered that we did not compare infants with and without using of analgesics. The reason for this is that it is not in accordance with our ethical principles. Another limitation is the low number of universe or that we did not compare SC with other scoring schemes of pain (e. i. PIPP), we compared it only with physiological parameters whose sensitivity and specificity, in relationship with objectification of pain perception, do not achieve of required level in infants.

ABBREVIATIONS

ASP, Area Small Peaks; AUC, Area Under Curve; GA, gestational age; GA-A, B, C, gestational age-group A, B, C; HR, heart rate; IASP, International Association of Study of Pain; PIPP, Premature Infant Pain Profile; PpS, Peak per Second; SatO₂, oxygen saturation; SC, skin conductivity.

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