Original article

Care to relieve pain-stress in preterm newborns

Caterina Di Gioia[1], Roberta Bracceschi[1], Cristiana Copioli[1], Benedetta Piccolo[1], Paola Ziliani[1], Francesco Pisani[1], Giulio Bevilacqua[2]

[1] Child Neuropsychiatric Unit, Neuroscience Department, University of Parma, Parma, Italy; [2] Department of Gynecological, Obstetric and Neonatological Sciences, University of Parma, Parma, Italy

Abstract. *Background and aim of the work:* A variety of non-pharmacological pain-prevention and relief techniques have been studied to evaluate the pain reduction in neonates. The aim of our study was to compare the analgesic effect of sucking a pacifier with the use of eutectic mixture of local anaesthetics (EMLA) during venipuncture in preterm newborns, using physiological and behavioural parameters as indicators of pain. *Methods:* We analysed the reaction to invasive procedures in 17 preterm newborns. Our patients underwent repeated vein draws without pain relief, sucking a pacifier, after the application of EMLA; we also evaluated a group of patients approached for care without pricking. For each infant we recorded the average values of the physiological parameters at rest and after pain stimuli, behavioural conditions (crying or grimaces), number and time required for blood draw. *Results:* The maximum heart rate values, respiratory rate, and the maximum respiratory rate values presented a statistically difference only between subjects that underwent vein draws compared to subjects without pricking ($p<0.01$). Moreover, the SpO_2 parameter presented a significant increase in the control group compared to the others ($p=0.024$). Analysis of behavioural parameters shows that crying seems significantly related to the duration and number of venipunctures ($p=0.000$). *Conclusions:* It is clear that pain stress is more closely related to the duration and number of venipuncture than pain relief methods. Our results suggest that limiting the number and duration of vein draws could help to reduce pain stress in preterm newborns.(www.actabiomedica.it)

Key words: preterm newborns, pain-prevention, EMLA, pacifier

Introduction

The progress made in perinatal care in recent years has changed the survival rates of very premature infants and neonates in critical conditions (1). Their health conditions and physiological instability need medical care with long-term invasive practices (1), which are often administered without anaesthesia or pain relief in Neonatal Intensive Care Units (NICU) (2).

The ability of the newborn and foetus to perceive and react to pain was recently acknowledged (3-5). Transmission of painful stimuli is present from a gestational age of 26 weeks and, at same time, the mechanisms that inhibit the transmission of painful stimuli are immature at birth, which suggests that newborns perceive pain in a more important way than adults (3).

Repeated painful stimuli in newborns may increase structural and functional damage and have permanent consequences that interfere in the development of the immature brain (6-9). The short-term effects of such stimuli include decreased oxygenation, haemodynamic instability or intracranial pressure (5, 10), and long-term sequelae include mother-infant bonding, sleep disorders, behaviour alterations, learning difficulties, hyperactivity/attention deficit disorder, altered sensitivity to pain and mental and rela-

tional disorders in childhood and adult life (8-9, 11-13).

The physiological parameters, which are routinely and easily obtainable and closely connected to the perception of pain in preterm infants' responses to acute pain, are increase heart and respiratory rates and decreased oxygen saturation (14, 15). Other clinical variables primarily used to evaluate their stress reaction are: intracranial pressure, palmar sweating variations and changes in cutaneous conductance, heart rate variability and hormonal alterations (5, 14, 16). Some of these physiological indicators may be affected by the underlying illness, making them less specific for pain (14).

Behavioural findings are considered the most sensitive indicator of acute and short-term pain in newborns (14): crying, facial expressions, vocalisation and body movements. However, behavioural pain assessment remains challenging and controversial due to the lack of a gold standard for neonatal pain expression (14), especially in preterm babies whose reactions are less conspicuous (15).

The treatment of neonatal pain during invasive procedures is therefore necessary for ethical reasons and in order to prevent long-term consequences.

A variety of non-pharmacological pain-prevention and relief techniques, used alone or in combination with pharmacological products, showed an effective reduction of the pain caused by minor procedures in neonates (6, 17).

Pain-relief methods that work by blocking the nociceptive transmission or activation systems that modulate pain include the use of oral sucrose-glucose, breastfeeding, and sucking a pacifier. Previous studies showed that non-nutritive sucking on a pacifier attenuates behavioural distress during painful procedures (10, 18-20). The exact mechanism by which pacifier relieve pain is yet to be identified.

Pharmacological treatment is rarely used due to concerns as to their efficacy and potential adverse effects in newborns. EMLA, an eutectic mixture of local anaesthetics, has been found to be an effective surface anaesthetic agent in children and infants. Some studies have shown that EMLA cream is also safe for neonates (21). In literature, authors differ in their conclusions regarding the effectiveness of EMLA-induced pain-relief at venipuncture in newborns (22, 23).

The aim of our study was to compare the analgesic effect of sucking a pacifier with the use of EMLA cream during venipuncture in preterm newborns, using physiological and behavioural indicators, and to evaluate which is most effective in preventing pain stress in preterm babies.

Materials and methods

We analysed the newborns' reaction to invasive procedures such as blood draws. Seventeen preterm newborns (8 females and 9 males) consecutively admitted to the University of Parma NICU between May 2006 and October 2006, with gestational age (GA) between 23 and 33 weeks (mean GA: 27.9 weeks), were enrolled in our study.

Children treated in the NICU often needed these procedures as part of their medical care, and we therefore considered it ethically correct to enrol them in our study.

Procedure

All blood draws were performed in the morning for clinical purposes and were carried out by a NICU nurse.

Our patients underwent repeated vein draws whilst in hospital, and the resulting data were therefore broken down as follows:

- ten painful events such as venipuncture using a sterile syringe without pain relief (group N);
- ten painful events such as venipuncture using a sterile syringe performed while the newborn was sucking a pacifier (group C);
- ten painful events such as venipuncture using a sterile syringe performed after the application of EMLA local anaesthetic cream (group E). Nurses applied one gram (1 ml of anaesthetic cream) to a 4 cm^2 area on the back of the baby's left hand. The cream was covered with an occlusive dressing and, after 15-20 minutes, the dressing and the substance were removed;
- we also considered ten non-painful events in which we recorded variations in physiological

parameters when the nurses approached the babies for care without pricking them (group A).

Our patients have never underwent an invasive procedure before this assessment.

Measurements

For each infant we recorded the following data:

1. Sex and gestational age.
2. Three physiological parameters: heart rate (HR), oxygen saturation (SpO2), respiratory rate (RR) at rest and after pain stimulus.
3. Number of blood samples taken and the success of venipuncture.
4. Total minutes required for blood draw, from the time the nurse approaches the child to when he/she leaves the newborn.
5. Behavioural conditions: facial actions such as crying or grimaces similar to crying; the presence or absence of these parameters were evaluated by NICU nurses who were more objective than parents and have greater expertise in describing the newborn's response to pain.

Physiological parameters were steadily monitored using trans-cutaneous electrodes (Arbo, Kendall) and trans-cutaneous oxymeter with a compact vital signs monitor (Hewlett Pachard, Neonatal Viridia) that allowed simultaneous monitoring of HR, SpO2 and RR variations.

Using this monitor, we registered the mean values per minute of each parameters while the maximum value of HR, RR and the minimum value of SpO2 were estimated throughout blood draw time.

Physiological parameters were recorded at four points:

1. Baseline: baseline conditions ten minutes before any procedure was performed on the newborn (named=T1)
2. Pre-procedural phase: three minutes before the stressful event (blood drawing or gentle care contact) (named=T 2)
3. Procedural phase: during the stressful event (named=T3)
4. Post-procedural phase: five minutes after the stressful event (named=T4)

Parameters referring to the stressful event were recorded from the 30 seconds before venipuncture to 30 seconds afterwards.

We separately obtained continuous, nominal or dichotomous data that were analysed as follows:

1. Variance analysis (ANOVA), of the nominal and the continuous variables.
2. Student t test of the dichotomous and the continuous variables.
3. χ^2 test among the dichotomous and nominal variables.

Results

Seventeen patients completed the study, all of whom underwent multiple blood draws. We divided the sample, according to the data obtained, into 4 groups, each one composed of ten evaluations.

Our groups had a homogeneous postnatal age (p=n.s.), but were unbalanced for GA because subjects belonging to the group A had significant lower GA than the other groups (p=0.003). Mean GA was 25.2 weeks in the group A, and was 27.9 weeks in the group N, 29.6 weeks in the group C and 29 weeks in the group E. However, GA was not statistically different (χ^2=2.57; gdl=4; p=NS) in the three experimental groups that underwent blood sampling (N, C and E).

The average values of the physiological parameters (HR, RR and SpO2) recorded in the pre-procedure, procedure and post-procedure phases are shown in Table 1.

Physiological parameters in the four groups at the four evaluation points:

SpO_2 value at baseline is significantly lower in group N (mean value 81.2%) (p=0.031) (Figure 1).

Physiological parameters in the procedural phase (T3) compared to baseline time (T1):

HR values increased in every experimental conditions: the increment in group E is significantly higher than in the other groups (p=0.003), which might be because the baseline HR values were already significantly lower (average=133.8 bs/m) (Figure 2).

The HR max, RR, and RR max present a statistically significant decrease in group A (p<0.01), and an increase in the other groups.

Table 1. Mean values of the physiological parameters (HR, RR and SpO2) in the pre-procedure, procedure and post-procedure phases.

	HR (bs/m) at T1	HR (bs/m) at T2	HR (bs/m) at T3	HR (bs/m) at T4	RR (r/m) at T1	RR (r/m) at T2	RR (r/m) at T3	RR (r/m) at T4	SpO2 (%) at T1	SpO2 (%) T2	SpO2 (%) at T3	SpO2 (%) at T4
Average of the whole sample	143,2	146,1	153,9	146,5	48,8	51,4	51,4	50,3	88	89,2	86,3	88,8
Average of the N group	142,8	146,5	151,8	148,3	43,0	43,7	50,4	47,7	81,2	87,4	85,3	87,6
Average of the C group	145,6	146,5	157,7	150,8	54,4	50,4	57,4	55,7	92,4	91,7	86,7	90,7
Average of the E group	133,8	141,7	154,3	138,5	48,9	55,0	54,6	50,2	90,8	91,5	89,2	92,0
Average of the A group	150,5	149,7	152,1	148,4	49,0	45,5	43,2	47,6	87,9	85,9	84,2	84,9

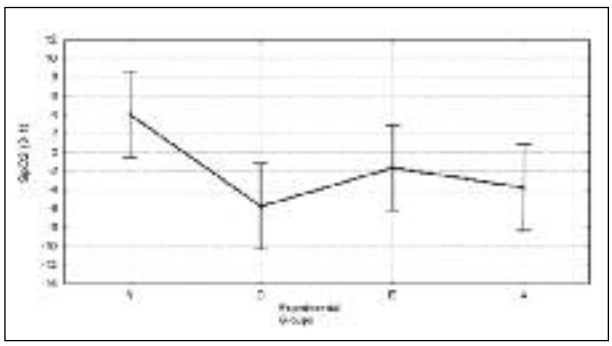

Figure 1. Variance of the SpO2 parameter from T1 to T3 in the four groups (p=0,024).
N=no-prevention Group; C=pacifier Group; E=EMLA Group; A=control Group

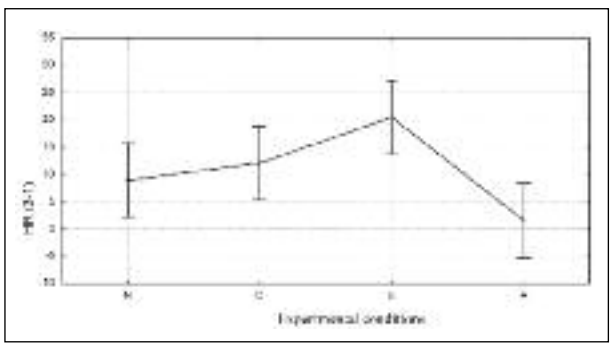

Figure 2. Variance of the HR parameter from T1 to T3 in the four groups (p=0,003).
N=no-prevention Group; C=pacifier Group; E=EMLA Group; A=control Group.

The SpO_2 parameter for group N presents a significant increase (p=0.024), probably due to the lower baseline value; whereas in groups C, E and A, we observed lower SpO_2 values at T3 since blood oxygenation values at T1 were higher.

Physiological parameters at T4 compared to T1:

According to HR and RR, the baseline values are recovered with the same rapidity in all four groups (p=n.s.). The SpO_2 value is higher for group N than for the other groups (p=0,036), because of a lower baseline SpO_2 value in this group.

Behavioural parameters:

We examined the presence/absence of the independent behavioural variable crying or grimaces similar to crying. Crying seems significantly related to the number of punctures and to the length of time needed for blood sampling (p=0.000) (Figures 3-4). Furthermore, subjects belonging to the lower GA group (p=0.011) and those with higher postnatal age (p=0.030) cried less.

Discussion

Physiological parameters such as an increase of HR and RR, and decrease in oxygen saturation pro-

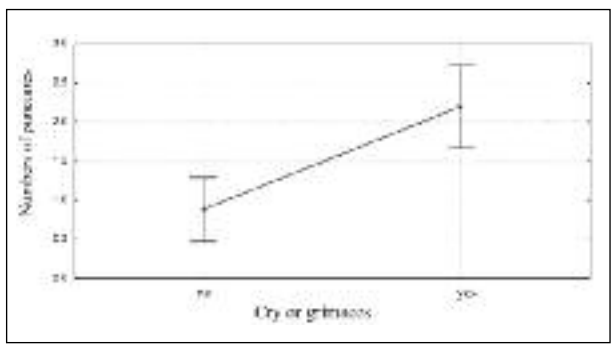

Figure 3. Relation between the number of venipunctures and presence of crying or grimaces (p=0,000).

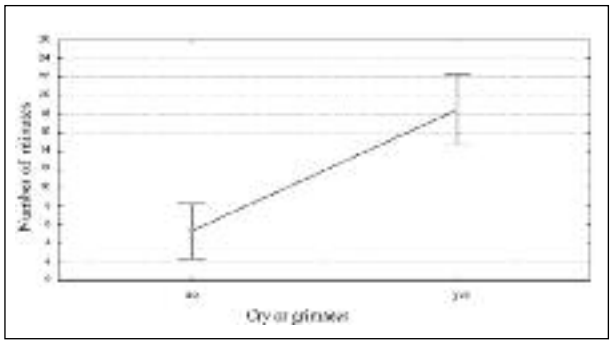

Figure 4. Relation between the duration of vein draws (minutes) and presence of crying or grimaces (p = 0,000).

vide information on preterm infants' responses to the stress evoked by acute pain. These variables are also routinely and easily obtainable and at the same time closely linked to the perception of pain (14, 15). In our study, we tested the changes in these parameters in two experimental conditions using ordinary care procedures. The use of EMLA cream or pacifier did not show significant differences compared to a group in which pain-relief methods was not used.

The physiological parameters of group A have a different trend than the common course in groups N, C, and E , which demonstrates that group A represented an effective control group (Table 1).

According to our results, two groups present significantly different baseline values, namely: HR for group E and the SpO_2 for group N.

Since group E shows lower baseline HR values and the same values as the other groups in the T3 phase, the variation in this parameter is clearly visible (Figure 2). Further investigation is required to establish whether this parasympathetic effect (22) is due to the systemic effect of EMLA absorbed by the skin.

On the other hand, group N subjects present lower basal SpO_2 values, and therefore a more significant increase of this parameter from the T1 to the T3 phases was expected (Figure 1). Group N is also homogeneous for GA and for baseline SpO_2 values. The observed phenomena may therefore be justified by emergency conditions requiring more rapid procedures without the use of any particular pain relief care than observed in the sample given a pacifier or treated with EMLA.

Analyzing both physiological and behavioural parameters of our patients, a clear efficacy of EMLA was not observed. This is in line with the literature where authors disagree in their conclusions regarding the effectiveness of EMLA (21-23).

Furthermore, from our data even the use of pacifier seems not useful in reducing the pain during stressful events in preterm newborns.

The analgesic effect of pacifier, when used alone or in combination with sucrose, has been demonstrated as useful in full-term newborns (10, 19-20), whereas the effectiveness of pacifier alone in preterm newborns is controversial (18, 25).

In our study, we tested the presence/absence of crying and grimaces similar to crying during vein draws. Crying is perhaps the most obvious response to pain in neonates and is acknowledged such as a valid measurement of pain in childhood (16, 24).

Older newborns cry significantly more than others. This suggested that older preterm infants have a greater perception of pain stimuli but they probably also assume more complete facial expressions that are easily identifiable by nurses. The younger preterm babies were also more likely to be treated with respiratory devices, that might reduce the newborns' facial expressions, which may also be less comprehensible to the operator. This result is in line with the results of other studies (15, 16) that affirm that most premature babies do not respond to pain as conspicuously as older infants. On the other hand, grimaces in preterm newborns reflected the perception of a painful event (20).

Moreover, neonates with a lower postnatal age and shorter hospitalisation times cry significantly less: probably, because they are in better health conditions than the newborns who are kept in hospital for longer and require greater care and life-support system use.

It is also important to point out that in our study crying is closely conditioned by the number and the time of vein draws in all groups (N, C, E) (Figure 3-4).

Conclusions

A combination of behavioural and physiological indicators gives the most complete information about acute pain in neonates.

In our study, the use of EMLA or pacifier seems not to be effective for the neonatal pain management.

Analysis of the behavioural parameters, on the other hand provided interesting data. Although this indicator is influenced by the newborn's health conditions and the observer's point of view, it shows that the neonates who underwent multiple venipunctures presented greater behavioural modifications, mainly in neonates with lower GA.

It is clear, from our data, that limiting the number and duration of vein draws must be the first commandment in order to reduce pain stress in preterm newborns in NICUs. This is possible by employing skilled, well qualified nursing staff whose expertise helps to prevent and to limit pain.

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Correspondence: Francesco Pisani
Child Neuropsychiatric Unit,
Department of Gynecological, Obstetric and
Neonatological Sciences, University of Parma
Via Gramsci 14
43100 Parma, Italy
Tel: + 39 0521 703741
Fax +39 0521 704708
E-mail: francesco.pisani@unipr.it