Original Article

Iran J Pediatr
Dec 2014; Vol 24 (No 6), Pp: 679-684

Do Term Newborns Respond Similarly to Different Painful Procedures?

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Received: *Oct 17, 2013*; Accepted: *Feb 16, 2014;* First Online Available: *Oct 31, 2014*

Abstract

Objective: Although many methods for pain assessment in newborns are available, none of them are widely accepted. Our aim was to answer the question: do newborns respond similarly to different painful procedures?

Methods: Sixty term newborns were involved in non-randomized prospective study. They were classified into 2 groups: Group A (n=30) who needed intubation and Group B (n=30) who necessitated umbilical vein catheterization. Close observation prior to and 10 minutes after the painful procedures was performed for recording of physiological and behavioral indicators. Plasma renin activity (PRA) was measured before and 10 minutes after the painful procedures.

Findings: There was statistically significant difference between the 2 groups as regards physiological and hormonal responses to pain ($P<0.05$). Apart from palmar sweating and crying, there was no significant difference in behavioral response ($P>0.05$). The median pre- and post-intubation levels of PRA were 3.04 and 12.05 ng/ml/hour, respectively. There was significant ($P<0.001$) increase of PRA after intubation. On the other hand, the median pre- and post-catheterization levels of PRA were 5.21 and 9.19 ng/ml/hour, respectively. There was significant ($P<0.001$) increase of PRA after umbilical vein catheterization. We found that PRA was the only indicator of pain in group A ($P=0.047$). On the other hand, we did not find any indicator of pain in group B.

Conclusion: We concluded that full-term newborns vary in their physiological and hormonal responses to different painful procedures but their behavioral response is the same.

Iranian Journal of Pediatrics, Volume 24 (Number 6), December 2014, Pages: 679-684

Key Words: Pain Assessment; Newborns; Plasma Renin Activity; Intubation; Umbilical Vein Catheterization

Introduction

Most infants in the neonatal intensive care-unit (NICU) are subjected to multiple and repeated minor painful procedures. Untreated pain in neonates may result in increased morbidity and length of stay in the NICU, exaggerated responses to pain in later life, and altered psychosocial development[1].

Accurate pain assessment is a central issue that confronts clinicians at the bedside of neonates or researchers who study nonverbal subjects. Although many validated methods for pain assessment are available, none of them are widely accepted or clearly superior to others [2]. Through assessment of response of newborns to pain after two painful procedures [endotracheal intubation (EI) and umbilical vein catheterization (UVC)]

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using multidimensional measurements (physiological, behavioral and hormonal), we aimed to answer the question: do newborns respond similarly to different painful procedures?

Subjects and Methods

Sixty term newborns of both sexes were involved in non-randomized prospective study. The patients subjected to painful procedures (EI and UVC) were recruited from NICU of Cairo University Children's Hospital (tertiary hospital). The study was conducted over 9 months' duration from March to December 2012.

Inclusion criteria were gestational age ≥37 weeks and recent admission to NICU (<1 day). The population of study was classified into 2 groups:

- Group A (n=30) which included newborns with respiratory distress who needed EI and mechanical ventilation.
- Group B (n=30) which included newborns with hyperbilirubinemia that reached a level necessitating insertion of UVC and exchange transfusion.

Patients with the following diagnoses were excluded from the study: lethal congenital anomalies, hypoxic ischemic encephalopathy, metabolic disorders that affect central nervous system (CNS) and hypertension. Also, patients or their breast-feeding mothers who received sedatives or hypnotics for any reason were excluded from the study.

Data were collected in the form of maternal history of drug intake, obstetric history of congenital infection, gestational age, mode of delivery, Apgar score at 1 and 5 minutes after birth, provisional diagnosis and time elapsed since admission.

Thorough clinical examination initially with special emphasis on Ballard score to determine gestational age. Close observation prior to and 10 minutes after performing the painful procedure for recording of: heart rate (HR), respiratory rate (RR), mean arterial pressure (MAP) [MAP = diastolic blood pressure (BP)+1/3 (systolic BP–diastolic BP)], oxygen saturation (SaO_2), palmar sweating, facial responses (grimace, brow bulge, eye squeeze, nasolabial furrows, and mouth opening), limb and body movements and crying.

Palmar sweating, facial responses and crying were observed for their presence (yes) or absence (no). Limb and body movements were assessed by observation of posture and body movements. Posture and tone were assessed by observation after touching the neonate's arm or leg and observation of clenched fists and toes. Body movements were assessed by observation of activity of arms and legs. The results of observation were categorized into either semiflexed attitude, diffuse body movements and withdrawal of lower limbs.

It should be noted that presence of these responses (yes) prior to and 10 minutes after the painful procedure to the same extent was considered negative response (no). Crying was considered significant (yes) only if it fulfilled the following criteria: short latency, longer duration of first cry cycle, higher fundamental frequency and greater intensity in the upper ranges.

Peripheral plasma renin activity (PRA) was measured by radioimmunoassay before and 10 minutes after the painful procedure. PRA was expressed as ng/ml/hour of generated angiotensin I. The normal range of PRA was 0.18-7.25 ng/ml/hour.

None of the patients had received any pain medications or other non-pharmacological interventions to relieve pain when performing the procedure according to our NICU protocols.

The study protocol was approved by the local ethics committee, and informed written consent was obtained from the parents of the patients.

Quantitative (Numerical) data were presented as mean and standard deviation values. Median with minimum and maximum was used to present PRA. Qualitative data were presented as frequencies. The differences between post-procedural and pre-procedural quantitative variables were referred to change and presented by median. *Paired T test* was used to compare pre and post variables within the same group. *Mann-Whitney* test was used to compare the change in the quantitative variables in both groups. *Chi square test* was used to compare qualitative variables between the groups. *Spearman's correlation coefficient* was used to determine significant correlations between quantitative data. The significance level was set at P<0.05. Statistical analysis was performed with SPSS 16.0 (statistical

Table 1: Characters of the studied patients

Parameter		Group A (ventilated) (n= 30)	Group B (exchange transfusion) (n= 30)	*P.* value
Gestational age (weeks) [median (SD)]		37.92 (0.61)	38.27 (1.22)	0.1
Postnatal age at time of study (days) [mean (SD)]		16.63 (8.82)	12.13 (2.74)	0.01
Sex	**Male**	22 (73.3%)	14 (46.7%)	0.3
	Female	8 (26.7%)	16 (53.3%)	
Mode of delivery	**NVD**	13 (43.3%)	14 (46.7%)	0.7
	CS	17 (56.7%)	16 (53.3%)	

NVD: Normal vaginal delivery; CS: Caesarian section; SD: Standard deviation

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Findings

A total of 60 newborns (36 males and 24 females) were included in this study. No statistical significant difference was found between the two groups as regards gestational age, gender and mode of delivery. The demographic data of the studied patients are shown in Table 1. The mean postnatal age at time of study for group A was 16.63 days while it was 12.13 for group B.

The median pre-intubation level of PRA was 3.04 ng/ml/hour (range: 0.74-7.25) while the post-intubation median level was 12.05 ng/ml/hour (range: 2.96-28.12). There was significant (P<0.001) increase of PRA after intubation. The median pre-catheterization level of PRA was 5.21 ng/ml/hour (range: 0.91-11.98) while the post-catheterization median level was 9.19 ng/ml/hour (range: 1.17-15.22). There was significant (P<0.001) increase of PRA after UVC. Comparison of other quantitative and qualitative variables is shown in Table 2, 3.

There was significant difference between the 2 groups as regards the change in HR, RR, MAP, SaO_2 and PRA (0.01, <0.001, <0.001, <0.001 and 0.002 respectively).

As regards PRA, we found a statistically significant correlation between post-intubation PRA and MAP (P=0.008) (Fig 1) but there was no significant correlation between post-intubation PRA and HR (P=0.9). On the other hand, there was no significant correlation between pre-intubation PRA and either HR or MAP (P=0.8 and 0.4, respectively).

We did not find a significant correlation between pre-catheterization PRA and either heart rate or MAP (P=0.7 and 0.7, respectively). Also, there was no significant correlation between post-catheterization PRA and either heart rate or MAP (P=0.2 and 0.8, respectively).

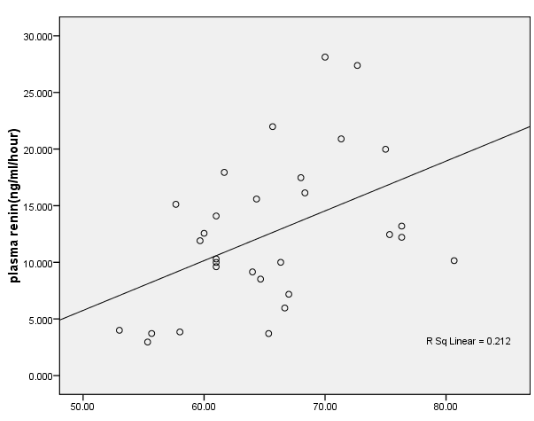

Fig. 1: Correlation between post-intubation plasma renin activity and mean arterial pressure

Table 2: Quantitative variables in the patients

Group	Parameter	Pre-intubation mean (SD)	Post-intubation mean (SD)	Change (median)	*P.* value
Group A (n= 30)	**HR (rate/minute)**	147.83 (8.02)	154.83 (6.62)	7.00	<0.001
	RR (rate/minute)	69.50 (7.15)	60.47 (3.20)	-8.00	<0.001
	MAP (mmHg)	54.65 (2.64)	65.43 (6.98)	10.00	<0.001
	SaO_2 (%)	76.83 (5.23)	90.77 (4.75)	14.00	<0.001
Group B (n= 30)	**HR (rate/minute)**	147.47 (10.20)	149.60 (10.74)	3.00	0.1
	RR (rate/minute)	48.73 (4.12)	47.27 (5.04)	-1.00	0.09
	MAP (mmHg)	61.55 (7.56)	63.22 (4.33)	2.33	0.2
	SaO_2 (%)	95.07 (2.31)	93.27 (3.10)	-2.00	0.07

HR: Heart rate; RR: respirateory rate; MAP: Mean arterial pressure; SaO_2: oxygen saturation; SD: Standard deviation

Discussion

There are several tools for assessment of pain in newborns such as PIPP (premature Infant Pain Profile), CRIES (Crying, Require Oxygen Saturation, Increased Vital Signs, Expression, and Sleeplessness), N-PASS (Neonatal Pain Agitation and Sedation Scale), NFCS (Neonatal Facing Coding system), NIPS (Neonatal Infant Pain Scale), PAT (Pain Assessment Tool), SUN (Scale for Use in Newborns), etc…. [3].

Intubation and UVC are 2 invasive NICU procedures that were found by many authors as the most painful procedures in NICU[4]. Our assessment included measurements of physiological indicators (HR, RR, MAP, SaO_2 and palmar sweating), behavioral indicators (facial expression: brow bulge, nasolabial furrows, mouth opening and grimace, body movements and crying) and hormonal indicators (plasma renin activity).

Up to our knowledge, this is the first study to compare the neonatal response to pain with different painful procedures. We found that neonatal physiological (HR, RR, MAP and SaO_2) and hormonal (PRA) responses to pain vary with the studied painful procedures. A drawback of the physiological indicators is that deviations may also be caused by the underlying illness[5]. Furthermore, daily medical interventions aim at keeping heart rate, blood pressure and oxygen saturation at acceptable levels without treating pain [3].

On the other hand, behavioral response to pain was the same with different painful procedures. Many authors found that facial expression is

Table: Qualitative variables in the patients

Parameter		Group A (n=30)	Group B (n=30)	*P.* value
Palmar sweating	Yes	14	22	0.03
	No	16	8	
Grimace	Yes	27	30	0.1
	No	3	0	
Brow bulge	Yes	27	30	0.1
	No	3	0	
Eye squeeze	Yes	27	30	0.1
	No	3	0	
Nasolabial furrows	Yes	27	30	0.1
	No	3	0	
Mouth opening	Yes	26	30	0.06
	No	4	0	
Body movement	semiflexed attitude	7	12	0.3
	Diffuse body movements	18	16	
	Withdrawal of lower limbs	5	2	
Crying	Yes	0	30	<0.001
	No	30	0	

generally considered the most sensitive indicator of pain in neonates [6, 7]. It should be noted that Gibbins et al found that the magnitude of facial responses to pain was proportional to gestational age with the youngest infants showing the least amount of change[8].

Pain assessment based on body movement is bound to present a misleading picture in the immobile painful infant[3]. Variable results were obtained in this context, some authors found that arm and leg movements change very little with painful procedure[9] while others found that body movements are an important indicator that discriminate pain from stress in preterm infants[10].

In concordance to our findings after intubation, most of researchers[7,8] found increased HR in response to acute pain that was associated with most of invasive procedures. However Stevens et al found that an infant's heart rate initially decreases and then increases in response to short, sharp pain during painful procedures such as circumcision, lumbar punctures, and intubations[11].

Also, in agreement with our results, Bhutada et al found acute increases in blood pressure in response to intubation in a study of 30 newborn infants who required semi-elective nasotracheal intubation[12]. Also, Carbajal et al found that tracheal intubation in awake preterm and full-term neonates causes a significant increase in arterial blood pressure[13].

Sympathetic responses are commonly associated with mild to moderate pain and this may explain the increase in HR and BP in response to pain, however, increases in heart rate due to acute pain may be short lasting and therefore often remain unnoticed. Changes in vital signs are less useful for chronic pain[3].

Decline of RR and improvement of SaO2 in newborns with respiratory distress after intubation go with logic and they should not be used for pain assessment in those patients.

It is well known that umbilical catheterization may be complicated by arrhythmias but assessment of the physiological markers 10 minutes after insertion of the catheter in our study may explain why there was no significant change of these indicators. Also, it should be noted that the severity of illness may cause less explicit pain reactions. Infants lacking energy due to the severity of their illness consequently are less capable of signaling pain[14].

In concordance to our results, Yilmaz F and Arikan D did not find significant change in SaO_2 with different painful interventions[15].

In agreement with many researchers, we found significant increase in PRA after the studied painful procedures[16,17]. It should be noted that newborn infants subjected to repetitive painful and stressful events during neonatal intensive care, the renin–aldosterone pathway may be found to increase but it decreases again over time[18]. It is not clear why PRA was correlated to MAP only after intubation and not in other situations (pre-intubation, pre- or post-catheterization).

PRA was found to be the single indicator of pain in group A (after exclusion of RR, SaO_2 and crying). On the other hand, we did not find any reliable indicator of pain in group B. Many researchers believe that an ideal pain indicator in neonatal period does not exist and physiological indicators are not specific[19,20].

One of the limitations of this study is the small number of studied patients which may be a statistical obstacle in finding more indicators of pain. Another limitation is the study of only 2 painful procedures. Further studies are needed on larger scale of patients with different painful procedures.

Conclusion

In conclusion, full-term newborns vary in their physiological and hormonal responses to different painful procedures but their behavioral response is the same. From our point of view, some commonly used tools for assessment of pain in newborns particularly RR and SaO_2 are not very helpful with every painful procedure.

Acknowledgment

The authors thank Prof. Reem Nabil, MD for her support.

Authors' Contribution

H. Sawires: Acquisition of data, data analysis, interpretation and manuscript preparation.

M. Abd-El Meguid and M. Ishak: Study design, concept and critical revision of the manuscript.
M. Abd-El Hady: Fund collection.
All authors approved the final version of the article.

Conflict of Interest: None

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