Original research article

Effect of maternal heart sounds on physiological parameters in preterm infants during aspiration

Dilek Küçük Alemdar [a] *, Fatma Güdücü Tüfekci [b]

[a] *Giresun University, Faculty of Health Science, Department of Midwifery, Giresun, Turkey*
[b] *Atatürk University, Faculty of Health Sciences, Department of Pediatric Nursing, Erzurum, Turkey*

ARTICLE INFO

ABSTRACT

Aim: The aim of this study was to evaluate the effect of maternal heart sound given to preterm infants during aspiration on pain and comfort.

Methods: This was a randomized controlled trial. Preterm infants ($n = 62$) receiving care or treatment at a neonatal intensive care unit (NICU) were eligible for participation in this study. Infants in the intervention group were provided with prerecorded maternal heart sounds before, during, and after aspiration, whereas infants in the control group received routine care.

Results: In both groups, the infants' physiologic parameters were evaluated during aspiration. In the study, it was determined that while there was an insignificant difference between the experimental group and the control group in terms of respiratory rate and heart rate averages before, during, and after the aspiration, there was a significant difference between them in terms of SO_2 averages before, during, and after the aspiration, and this significance arose from the experimental group.

Conclusion: Considering the positive effect of maternal heart sound given to preterm infants during aspiration, we recommend that this method can be used in NICU.

Introduction

Invasive procedures are common sources of pain in newborns [1, 2]. Suctioning is an invasive procedure often applied by nurses in the care of patients treated with mechanical ventilation [3]. During the stressful process of suctioning, infants are observed to exhibit the same physiologic responses encountered in other painful procedures. Using pacifiers or sucrose solutions or swaddling the baby may be used during the suctioning to help to relieve the pain. In addition, opioids may be administered through continuous intravenous infusion or slow injection [1].

In the NICU, the endotracheal aspiration, which is among the painful interventional procedures applied by nurses, is defined as the mechanical cleaning process of the pulmonary secretions of patients with an artificial airway [4, 5]. A painful procedure such as aspiration adversely affects newborns' physiological parameters, comfort, sleep, development and the length of hospital stay [6]. There have been many studies on aspiration in recent years [3, 7–14].

* **Corresponding author:** Dilek Küçük Alemdar, Pediatric Nurse, PhD, Assist. Prof., Giresun University, Faculty of Health Science, Department of Midwifery, Yenimahalle, Lise Caddesi, 28340 Piraziz-Giresun, Turkey; e-mail: dilekkucuk@atauni.edu.tr

All sense organs in the fetus begin to develop during the prenatal period and generally develop in the following sequence: tactile, vestibular, chemical, auditory, and visual sense organs. Hearing typically starts in the 18th week of pregnancy and matures by approximately the 28th week. Fetal response to sound begins in the 26th–28th week [15]. During the 30th–35th gestational weeks, the fetus can hear the mother's voice, responds to her sounds, and differentiates her sound from the others [16].

Auditory stimuli such as structured, rhythmical, cardiovascular, and patterned bowel sounds occur in the intrauterine environment and consist of sounds such as the patterning of placental musical sounds [16]. Sounds arising from the mother's body include sounds from respiration, cardiovascular system, intestinal activities, and body movements. An average noise level of 50 decibels (dB) arises within the uterus. Furthermore, low-frequency sounds from the environment are more audible to the fetus, and the fetus learns about its mother's voice or the external music played. Both the fetus and the neonate may become accustomed to a sound that they have heard several times [17]. Voice control positively affects communication of infants with their families' as much as physiological stability, age-appropriate sensory development, and growth [17, 18]. The American Academy of Pediatrics recommends that sound levels in the NICU should not exceed 45 dB [19–21].

It is a great problem for preterm neonates who are separated from the mother's voice, which is an important source for the development of sound sensation of the fetus, to be exposed to intense sound stimuli in NICU. The fetus is normally familiar with blood flow sound, bowel movements, the mother's heartbeat sound, the mother's voice and movements, and synchronized sounds in the uterus [22]. The environment of NICU has very high environmental and human-made sounds. As a result of unwanted noise in NICU; numerous stress behaviors such as fatigue, stress, hyperalertness, fear etc., as well as physiological changes; changes in heart rate, oxygen saturation level, respiratory rhythm, and blood pressure, increase in intracranial pressure, and changes in corticosteroid hormone are observed. However, an effective auditory stimulus occupies the infant, and provides a cognitive effect for pain control, physiological stability and suppressing the pain response [20, 23–26].

The purpose of this experimental study was to determine the effect maternal heart sounds played on preterm infants' physiologic parameters during the aspiration procedure.

Materials and methods

This was a randomized, single-blind experimental study. The study population consisted of preterms, fulfilling the selection criteria, who received treatment and care in the Hospital's NICU in Turkey, between July 2012 and February 2013. The study was conducted with 62 preterm infants, randomly divided into the experimental (n = 32) and the control (n = 30) groups. In the power analysis performed to determine the sample size, the calculated sample size was found to be 62 preterms in order to achieve a 0.90 power in the test, at a significance level of 0.05 with a medium level of effect.

Selection criteria for the study group

The criteria of the study group were: Infants with gestational age ≥28 weeks and ≤36 weeks; who had no congenital anomalies; required tracheal aspiration; underwent at most three tracheal aspirations after the intubation process; had spontaneous breathing and needed mechanical ventilation support; and had not been given any pharmacological or non-pharmacological pain reliever before the procedure, were included in the study.

Measuring instruments

Preterm Infant Introductory Information Form – includes items on the newborn's age, gender, gestational age, birth weight, length, head circumference, Apgar score, nutritional status (breastfeeding and/or formula feeding) and its diagnostics. Additionally, it is a form developed for the purpose of recording these measurements to evaluate the effect of interventions made before, during and after the aspiration on oxygen saturation, heart rate, and respiratory levels of premature infants.

Intervention

Preterms admitted to the NICU were evaluated in accordance with the selection criteria for the study group. The preterm infants supported for mechanical ventilation are not sedated in the studied unit. The aspiration process was performed with aspiration-catheter no. 6 in preterm infants born between 28 and 34 weeks of gestation, and catheter no. 7 was used in 34–38 week-old preterm infants at 100 mmHg pressure. Oxygen at 100% concentration was applied before and after the procedure. The aspiration procedure was carried out in 10 seconds. All of the aspiration procedure was performed by the same nurse working in the day shift. Families of the infants were informed about the research, and the infants were included in the study after obtaining the consent of the families who agreed to participate. It was stated to the families that the data will be confidential and will only be used for this research.

In the study, preterm infants who had spontaneous breathing, but needed respiratory support through application of mechanical ventilation were included in the study during one of the three aspiration needed. In order to record the heart sounds of the mothers, whose babies were included in the experimental group, the maternal heart sounds were recorded using a hand doppler and an MP3 player. Then, these records were played for infants through a speaker set to 45 dB. Maternal heart sounds were played for the babies for 15 min prior to aspiration, during the aspiration and again for 15 min after the aspiration. Heart rate and SO_2 were recorded from the monitor and the respiratory rate was counted by the researcher for 1 min.

The preterm infants in control group did not receive any additional interventions during one of the three aspiration requirements in the clinic. Heart rate and SO_2 were recorded from the monitor and the respiratory rate was counted by the researcher for 1 min.

Data analysis

Data were analyzed using the SPSS (Statistical Package for Social Sciences) 18.0 and R 2.15.2 statistical analysis software packages. Percentage distribution, mean, standard deviation, chi-square, Kolmogorov–Smirnov Z test, and t-test comparison between groups were used for the statistical analysis of the data.

Ethical considerations

The legal permission of the related institution and ethical consent No 2012.3.1/9 from the Ethics Committee of University, Faculty of Health Sciences in July 24, 2012 was obtained in order to conduct the study. The purpose of the study was explained to the families of the premature infants included in the study, their questions were answered and written consents were obtained. Parents were informed that the information they had given would be confidential and would not be used anywhere else. In the study, the related ethical principles of "Informed Consent Policy", "Volunteer Policy" and "Privacy Protection Policy" has been fulfilled since the use of human subjects requires the protection of individual rights.

Results

In the study, no statistically significant difference was found between the preterm infants in the control and experimental groups in terms of gender, gestational age, birth weight, birth height, birth head circumference, diet, the Apgar score at the 5th minute and diagnosis averages ($p > 0.05$, Table 1, 2). A statistically significant difference was only found in the 1st minute Apgar score variable between the infants in the experimental and control group. These results indicate that the experimental and control groups were similar in terms of control variables except the 1st minute Apgar score ($p < 0.05$, Table 1, 2).

Table 1 – Comparison of descriptive characteristics of the experimental and control groups (n = 62)

Characteristics	Groups				Test/p
	Experimental (n = 32)		Control (n = 30)		
	n	%	n	%	
Gender					
Girl	9	28.1	13	43.3	χ^2 = 1.56 $p > 0.05$
Boy	23	71.9	17	56.7	
Birth					
Spontaneous	1	3.1	3	10.0	χ^2 = 1.213 $p > 0.05$
Section	31	96.9	27	90.0	
Diet					
TPN[a]	1	3.1	4	13.3	χ^2 = 2.17 $p > 0.05$
IV Infusion	31	96.9	26	86.7	
Diagnosis					
RDS[b]	31	96.9	28	93.3	χ^2 = 0.42 $p > 0.05$
RDS + IUGR[c]	1	3.1	2	6.7	

[a] Total parenteral nutrition.
[b] Respiratory distress syndrome.
[c] Intra uterine growth retardation.

Table 2 – Comparison of descriptive characteristics of the experimental and control groups (n = 62)

Characteristics	Groups		Test/p
	Experimental (n = 32)	Control (n = 30)	
	Mean ± SD	Mean ± SD	
Gestational age	33.63 ± 3.32	32.23 ± 1.17	t = 1.68 $p > 0.05$
Birth weight (gr)	2265.65 ± 780.74	1886.83 ± 803.57	t = 1.86 $p > 0.05$
Birth head circumference (cm)	32.90 ± 5.22	30.78 ± 3.36	t = 1.89 $p > 0.05$
Birth height (cm)	45.28 ± 5.27	43.13 ± 5.12	t = 1.58 $p > 0.05$
	M ± IQR	M ± IQR	
Apgar score 1 min	7.00 ± 3.75	4.00 ± 3.25	KSz = 1.55 $p > 0.05$
Apgar score 5 min	8.00 ± 3.00	6.50 ± 2.00	KSz = 1.03 $p > 0.05$

It was found that while heart rate averages were 136.41 ± 18.67 before the procedure, 147.00 ± 18.64 during the procedure, and 145.97 ± 17.03 after the procedure in the experimental group; they were 141.53 ± 12.49 before the procedure, 155.47 ± 16.16 during the procedure, and 154.60 ± 18.13 after the procedure in the control group and the difference between the groups was statistically insignificant ($p > 0.05$, Table 1, 2). There was a statistically significant difference between the experimental and control groups in terms of heart rate averages before, during, and after the procedure ($p < 0.05$, Table 3).

Table 3 – Comparison of the average HR score between the experimental and control groups

Heart rate (HR)[a]	Groups		Test/p	
	Experimental (n = 32)	Control (n = 30)		
	Mean ± SD	Mean ± SD		
HR before aspiration	136.41 ± 18.67	141.53 ± 12.49	$t = -1.26$	$p > 0.05$
HR during aspiration	147.00 ± 18.64	155.47 ± 16.16	$t = -1.90$	$p > 0.05$
HR after aspiration	145.97 ± 17.03	154.60 ± 18.13	$t = -1.93$	$p > 0.05$
[a] The number in a minute.				

It was determined that while respiratory rate averages were 45.25 ± 9.51 before the procedure, 32.63 ± 8.89 during the procedure, and 42.41 ± 7.41 after the procedure in the experimental group, in the control group were 45.10 ± 11.56 before the procedure, 32.80 ± 9.89 during the procedure, and 41.80 ± 10.11 after the procedure, and the difference between the groups was statistically insignificant ($p > 0.05$, Table 4).

Table 4 – Comparison of the average respiration score between the experimental and control groups

Respiratory rate[a]	Groups		Test/p	
	Experimental (n = 32)	Control (n = 30)		
	Mean ± SD	Mean ± SD		
RR before aspiration	45.25 ± 9.51	45.10 ± 11.56	$F = 0.056$	$p > 0.05$
RR during aspiration	32.63 ± 8.89	32.80 ± 9.89	$F = 0.073$	$p > 0.05$
RR after aspiration	42.41 ± 7.41	41.80 ± 10.11	$F = 0.271$	$p > 0.05$
[a] Breaths per minute.				

It was determined that SO_2 averages were 96.59 ± 3.08 before the procedure, 93.19 ± 4.58 during the procedure, and 95.66 ± 3.42 after the procedure in the experimental group; whereas, they were 96.20 ± 3.95 before the procedure, 87.50 ± 6.56 during the procedure, and 91.17 ± 6.08 after the procedure in the control group, and the difference between the groups in terms of SO_2 averages was statistically significant during and after the procedure ($p > 0.05$, Table 5). It was found that the significant difference arising between the experimental group and the control group in terms of SO_2 averages was caused by the experimental group (according to Post hoc advanced analysis results). SO_2 before the procedure was lower than the saturation during the procedure at a statistically significant level and SO_2 after the procedure was lower than the saturation during the procedure at a statistically significant level. SO_2 average was the lowest during the procedure.

Table 5 – Comparison of the average SO_2 level score between the experimental and control groups

SO_2	Groups		Test/p	
	Experimental (n = 32)	Control (n = 30)		
	Mean ± SD	Mean ± SD		
SO_2 before aspiration	96.59 ± 3.08	96.20 ± 3.95	$F = 0.439$	$p > 0.05$
SO_2 during aspiration	93.19 ± 4.58	87.50 ± 6.56	$F = 3.979$	$p > 0.05$
SO_2 after aspiration	95.66 ± 3.42	91.17 ± 6.08	$F = 3.612$	$p > 0.05$

Discussion

In the study, it was determined that HR and respiratory rates of infants in the experimental group and the control group showed a distribution within normal limits before, during, and after aspiration; HR was 136–147 and respiratory rate was 32–45/min. for the experimental group, and HR was 141–155 and respiratory rate was 32–45/min. in the control group, but the difference between the groups was not statistically significant ($p > 0.05$, Tables 3, 4). Additionally, HR increased and respiratory rate decreased during the procedure in both groups. In the literature [27] it is stated, that for a premature neonate it is required to have a HR between 100–180/min and a respiratory rate between 30–60/min. In preterm infants, the respiratory rate is more unstable compared to term newborns and a tendency toward apnea is observed [28]. In the study, SO_2 rates of infants in the experimental group showed a distribution between 93 and 96, and SO_2 rates of infants in the control group showed a distribution between 85 and 98. It was determined that there was a statistically significant difference between SO_2 averages of the infants in the experimental and control groups during and after the aspiration ($p < 0.05$, Table 5). In the literature [27] it is stated, that the confidence interval of SO_2 values of premature neonate needs to be between 95 and 100. These results supported the hypothesis that "physiological parameters of preterm infants who listened to the mother's heartbeat sound before, during, and after the aspiration are within normal limits" in respect of SO_2.

It is a known fact that the infant is affected by the mother's heartbeat in the mother's womb, and after the birth, hearing this familiar sound and rhythm again enables a soothing effect. In the experiments, newborn infants who stayed in the room with the taped sound of the uterus fell asleep earlier than those in the room without the mentioned sound [24, 29].

In the study conducted by Segall [30], who investigated the effect of auditory stimulus on the cardiovascular system, it was determined that in terms of HR, there was a significant difference between the infants who listened to the mother's voice and the group listening to another woman's voice and the group listening to no voice. Similarly, in the study conducted by Türker [31] it was found, that there was a significant difference between respiratory rate averages of newborns, who listened to white noise and those of control group before and after invasive intervention. In the present study, there was no significant difference between the groups in terms of HR and respiratory rate. The results of the study show no similarity with these results.

In the study conducted by Colins and Khuck [32] it was found, that during the aspiration procedure made on intubated preterm infants, the SO_2 levels of infants who listened to the sound of the intrauterine environment were higher compared to the control group. In other studies [7, 33] examining the effect of musical therapy during endotracheal aspiration on SO_2 among preterm infants who were administered with endotracheal intubation, the SO_2 values of infants in the group listening to the music returned to normal values faster compared to those who did not listen to music. In the study of Schwartz [34], the preterm newborns listened to soothing music similar to a mother's voice and uterus's voice in intervals. It was observed that listening to music positively affected the vital signs of preterm infants by providing a decrease in stress indications. The results of the study show similarity with these results.

In the literature, there are studies that investigate the effect of listening to mother's heartbeat sound on stress behaviors. In the study conducted by Kurihara et al. [35] stress behaviors of newborns were examined and it was observed that there was a significant decrease in stress behavior scores of the group listening to mother's heartbeat compared to the group who listened to Japanese drum sounds and the group who did not listen to anything. Again in the study conducted by Doheny et al. [36], who evaluated the therapeutic effect of listening to a mother's heartbeat sound and mother's voice on cardiorespiratory system in premterm infants, it was determined that the group who listened to the mother's heartbeat sound had lower apnea and bradycardia.

In the study conducted by Johnston et al. [37], it was reported that SO_2 values of preterm infants who listened to mother's voice during the heel lance were higher at a significant level compared to the control group, however it had no significant effect on the pain. The results of the study show similarity with these results.

Conclusion

The summary of results obtained in this experimental study determine that there was an insignificant difference between the respiratory rate and HR averages before, during, and after the aspiration, and there was a significant difference between them in terms of SO_2 averages during and after the procedure, and this significance was associated with the experimental group. Considering the positive effect of maternal heart sound given to preterm infants during aspiration, we recommend that this method be used in NICU.

Conflict of interests

The authors declare that they are not aware of any conflicts of interest regarding this article.

Acknowledgements

REFERENCES

[1] Anand KJS, International Evidence-Based Group for Neonatal Pain. Consensus statement for the prevention and management of pain in the newborn. Archives of Pediatrics and Adolescent Medicine 2001;155(2):173–80.

[2] Dinçer İ, Yurtçu M, Günel E. Pain in newborns and nonpharmacologic treatment procedures. Journal of Selçuk University Medicine 2011;27:46–51.

[3] Özden D. Bir devlet hastanesinde açık ve kapalı sistem aspirasyon yöntemleri için standart geliştirilmesi ve bu yöntemlerin hastaların hemodinamik durumuna etkisinin belirlenmesi. Doctoral dissertation. Ankara: Hacettepe University; 2007.

[4] American Association of Respiratory Care (AARC). AARC Clinical Practice Guidelines. Endotracheal suctioning of mechanically ventilated patients with artificial airways 2010. Respiratuar Care 2010;55(6):758–64.

[5] Celik S. Mechanical ventilation of the patient care. Journal of the Turkish Society of Critical Care Nurse 2006;10:19–25.

[6] Anand KJS. Pain assessment in preterm neonates. Pediatrics 2007;119(3):605–7.

[7] Chou LL, Wang RH, Chen SJ, Pai L. Effects of music therapy on oxygen saturation in premature infants receiving endotracheal suctioning. Journal of Nursing Research 2003;11(3):209–16.

[8] Trevisanuto D, Doglioni N, Zanardo V. The management of endotracheal tubes and nasal cannulae: The role of nurses. Early Human Development 2009;85 (10 Suppl):S85–7.

[9] Thomas M, Fothergill-Bourbonnais F. Clinical judgements about endotracheal suctioning: what cues do expert pediatric critical care nurses consider? Critical Care Nursing Clinical North America 2005;17(4):329–40.

[10] Morrow BM, Argent AC. A Comprehensive review of pediatric endotracheal suctioning: Effects, indications and clinical practice. Critical Care Medicine 2008;9(5):465–77.

[11] Sönmez DD, Kuğuoğlu S. Assessment of pain during endotracheal suction in the pediatric intensive care unit. Pain Management Nursing 2015;16(1):11–19.

[12] Ward-Larson C, Horn RA, Gosnell F. The efficacy of facilitated tucking for relieving procedural pain of endotracheal suctioning in very low birthweight infants. American Journal of Maternal Child Nurse 2004;29(3):151–6.

[13] Axelin A, Salantera S, Lehtonen L. Facilitated tucking by parents' in pain management of preterm infants – a randomized crossover trial. Early Human Development 2006;82(4):241–7.

[14] Arroyo-Novoa CM, Figueroa-Ramos MI, Puntillo KA, Stanik-Hutt J, Thompson CL, White C, Wild LR. Pain related to tracheal suctioning in awake acutely and critically ill adults: a descriptive study. Intensive Critical Care Nursing 2008;24(1):20–7.

[15] Graven SN. Sound and developing infant in the NICU. Journal of Perinatology 2000;20(8s):S88–S93.

[16] Neal DO. Music as a health patterning modality for preterm infants in the NICU. Dissertation thesis. Minnesota: Faculty of the graduate school of the University of Minnesota; 2008.

[17] Nair MNG, Gupta G, Jatana SK. NICU Environment: Can we be ignorant? Medical Journal Armed Forces India 2003;59(2):93–5.

[18] Stewart K. Patterns: A Model for evaluating trauma in NICU music therapy. Part I – theory and design. Music and Medicine 2009;1(1):29–40.

[19] American Academy of Pediatrics, Committee on environmental health. Noise: a hazard for the fetus and newborn. Pediatrics 1997;100(4):724–7.

[20] Chen HL, Chen CH, Wu CC, Huang HJ, Wang TM, Hsu CC. The influence of neonatal intensive care unit design on sound level. Pediatr Neonatol 2009;50(6):270–4.

[21] Hodges AL, Wilson LL. Effects of music therapy on preterm infants in the neonatal intensive care unit. Alternative Therapies 2010;16(5):72–3.

[22] Krueger C. Exposure to maternal voice in preterm infants. Advances in Neonatal Care 2010;10(1):13–18.

[23] Johnston CC, Filion F, Nuyt AM. Recorded maternal voice for preterm neonates undergoing heel lance. Advanced Neonatal Care 2007;7(5):258–66.

[24] Standley JM. Music therapy for the neonate. Newborn and Infant Nursing Reviews 2001;1(4):211–16.

[25] Yılmaz G, Gürakan B, Saatçi Ü. Topuk kanı alınma sonrası bebeklerin ağlama sürelerine etki eden faktörler. Çocuk Sağlığı ve Hastalıkları Dergisi 2002;45:233–6.

[26] Tari KA. Yenidogan Yoğun Bakım Ünitelerinde Çevrenin Değerlendirilmesi ve Düzenlenmesi. In: Pek H (Ed.). Yoğun Bakım Ünitelerinde Bireyselleştirilmiş Destekleyici Gelişimsel Bakım Kursu. İstanbul; 2003.

[27] Cavuşoğlu H. Çocuk Sağlığı Hemşireliği. Ankara:Sistem Ofset Basımevi; 2008, pp. 64–8.

[28] Savaşer S, Yıldız S. Hemşireler için çocuk sağlığı ve hastalıkları öğrenim rehberi. İstanbul: İstanbul Tıp Kitabevi; 2009, pp. 51–8.

[29] Ovalı F. Fetüs ve yenidoğanda işitme: Temel Kavramlar ve Perspektifler. Türkiye Klinikleri Journal of Pediatr 2005;14:138–49.

[30] Segall M. Cardiac responsivity to auditory stimulation in premature infants. Nursing Research 1972;21(1):15–19.

[31] Türker F. Yenidoğan ağrı algısına beyaz gürültü ve Kucağa Almanın Etkisi, Sağlık Bilimleri Enstitüsü, Çocuk Sağlığı ve Hastalıkları Hemşireliği Anabilim Dalı, Unpublished master dissertation. İstanbul: Marmara University Institute of Health Sciences; 2010.

[32] Collins SK, Kuck K. Music therapy in the neonatal intensive care unit. Neonatal Network 1991;9(6):23–6.

[33] Burke M, Walsh J, Oehler J, Gingras J. Music therapy following suctioning: four case studies. Neonatal Network 1995;14(7):41–9.

[34] Schwartz FJ. Music stres reduction and medical cost savings in the neonatal intensive care unit. Journal of Prenatal and Perinatal Psychology Health 1997;12(1): 19–29.

[35] Kurihara H, Chiba H, Shimizu Y, Yanaihara T, Takeda M, Kawakami K, Takai-Kawakami K. Behavioral and adrenocortical responses to stress in neonates and the stabilizing effects of maternal heartbeat on them. Early Human Development 1996;46(1–2):117–27.

[36] Doheny L, Hurwitz S, Insoft R, Ringer S, Lahav A. Exposure to biological maternal sounds improves cardiorespiratory regulation in extremely preterm infants. Journal of Maternal-Fetal and Neonatal Medicine 2012;25(9):1591–4.

[37] Johnston CC, Stevens B, Pinelli J, Gibbins S, Filion F, Jack A, et al. Kangaroo care is effective in diminishing pain response in preterm neonates. Arch Pediatr Adolesc Medicine 2003;157(11):1084–8.