



EVALUATION OF PERCEPTION OF EXTEROCEPTIVE SENSATIONS IN PRETERM NEONATES-A PILOT STUDY

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ABSTRACT

Aim: Preterm infant is deprived of various in-utero sensory experiences which have been documented as risk factor for prevalence of broad range of neurodevelopmental impairment in preterm infants. The present study evaluates the pain processing pattern in preterm neonates with and without known abnormalities using the Premature Infant Pain Profile (PIPP) - a 7 indicator pain measure that include three behavioural (facial actions: brow bulge, eye squeeze and nasolabial furrow), two physiological (heart rate and oxygen saturation), and two contextual (gestational age and behavioural state).

Method: Neonates were randomly observed for receiving one of the following procedures: Dry cotton swab for simple touch (T), Cold and warm water wet cotton swabs for recording temperature perceptions (Tp), venous puncture in the back of the hand (P), considered as a painful stimulus; or alcohol swab friction on the back of the hand (F), considered as a distressing but not painful stimulus. A neonatologist evaluated physiologic and behavioral pain parameters. The evaluation of the perception includes utilizing Neonatal Infant Pain Scale (NIPS) and PIPP.

Results: The mean pain score is 8.04 which is considered as moderate as per PIPP table. The standard deviation is 3.517. The probability distribution of pain is normal.

Conclusion: The pain perception according to the recorded score is moderate in the premature neonates and the perception score is comparatively high in preterm neonates with known abnormalities. The infants born at 29–31 weeks of gestational age group showed greatest changes in the hemodynamic patterns during exteroceptive painful stimulation.

KEY WORDS: premature, neonates, Premature Infant Pain Profile, PIPP, Neonatal Infant Pain Scale, NIPS, preterm birth.

INTRODUCTION

Preterm infant is deprived of various in-utero sensory experiences which have been documented as a risk factor for prevalence of a broad range of neurodevelopmental impairment in preterm infants.¹ The spectrum of neurodevelopmental disabilities includes cerebral palsy, mental retardation, visual and hearing impairments and more subtle disorders of central nervous system function.²

The Neonatal Intensive Care Unit [NICU] is one of the most commonly used clinical interventions in the stabilization and providing a multimodal sensory experience for normal growth and development of a preterm infant. In two decades, many pain assessment tools have been established to measure pain in infants in the NICU.³⁻⁷ Regrettably, the developed scales has not been upheld to



perform complete psychometric testing. Furthermore, many studies have not used appropriate theoretical models to determine the developmentally relevant, relatively specific pain indicators in this population.

According to Jonsdottir et al,⁸ the need for a pain measure is a clinically important issue for substantiating a therapeutic decision and evaluating the effectiveness of a particular intervention. This is especially true as professionals are becoming increasingly aware of the immediate and long-term effects of pain in preterm and term infants. The management of pain in infants at the NICU has improved over the last decade in response to advancements in the understandings of pain and pain relief although much is still to be learned.^{9,10} One of the major challenges is assessing the degree of experienced pain in the absence of verbal expression.⁹ The assessment of pain in the neonates needs more than a single indicator because nociception have much more complex nature in infants. There are two familiar indicators used for the pain assessment, One of which is the Premature Infant Pain Profile (PIPP). This is an indicator in English in 1990s and got to light in 1996 by Stevens and colleagues. This scale helps researchers and clinical practitioners to assess acute pain in preterm and term neonates.¹¹ The present study evaluates the pain processing pattern in preterm neonates with and without known abnormalities. The study also establishes evidence on gender differences in pain perception and level of alertness in preterm neonates for understanding the pain perception.

MATERIALS AND METHODS

This cross sectional study was conducted in the Neonatal Intensive Care Unit [NICU] & Paediatrics department of MGM Medical College, Navi Mumbai. A study population of 125 premature neonates was selected based on convenient sampling technique (admitted into neonatal ICU) and were separated into two groups based on the complications they possess. First group contained only preterm neonates without any known complication & the second observed group of preterm neonates possessed any known or observed birth complications such as gross or physiological defects.

Normal neonates were analyzed for any significant difference with the premature neonates. After written maternal consent prior to enrollment, healthy neonates admitted to rooming-in with their mothers, with post-natal age greater than 24 hours. At this time their stress response to delivery is attenuated; newborn preterm infants with late non-hemolytic jaundice and indication for venous puncture for bilirubin dosage by the clinical staff were selected and 30 to 45 minutes interval was given between last feeding and recorded observations in order to have a calm and reactive patient to observe.

The infants whose mothers had used any opioid during pregnancy, labor or delivery, were excluded in the study since these drugs can cross the placenta and affect fetus and newborn infant pain perception. Also with mothers who had general anesthesia during delivery were excluded, as anesthetics can readily cross the placenta and interfere with neonatal nociception; Infants at high risk due to major malformation or neurological abnormalities were also excluded from the study.

All the study population was exposed to various exteroceptive sensations like simple touch, pressure, pain, temperature and reaction of the neonates during exteroceptive sensation perception was noted.

After patient enrollment, the following neonatal data was registered: birth weight in grams, gestational age, gender, relationship between birth weight and gestational age, post-natal age in hours, and minutes after the last feeding.

Neonates were randomly observed for receiving one of the following procedures: Dry cotton swab for simple touch (T), Cold and warm water wet cotton swabs for recording temperature perceptions (Tp), venous puncture in the back of the hand (P), considered as a painful stimulus; or alcohol swab friction on the back of the hand (F), considered as a distressing but not painful stimulus.⁽³⁾ A neonatologist was assigned to evaluate the physiologic and behavioral pain parameters and the same was done.

After identification, the recruited infant, it was ensured that the subject has completely settled with the environment. A pulse-oximeter was connected to neonates of which the probe was placed on the foot. The neonates were then allowed to rest for five minutes prior to procedure. After completion of procedure, the subjects were observed for 10 minutes.

All the parameters were measured before (PRE) the procedure, and was repeated during (T0) the procedure. The assessment was also done after one minute (T1), three minutes (T3), five minutes (T5) and ten (T10) minutes of the procedure. The evaluation of the perception includes utilizing NIPS¹² [Neonatal Infant Pain Scale] the Premature Infant Pain Profile [PIPP] ¹¹scales for identifying the variability.

RESULTS

Out of 125 participating neonates, 73 were born vaginally and 52 with caesarian section. The normal group in contrast to preterm neonates showed minimal pain perception. The mean gestational age was 31.4 weeks (26-38) and the mean birth weight 1.541gms.



Modes of oxygenation include CPAP, Oxygenation by hood and Ventilator. The percentages of neonates depending on different modes of oxygenation are represented in Graph-1. Table-1 shows the descriptive statistics of birth weight for neonates.

The preterm neonates based on gestational week born, were grouped into 5 groups (Table-2) with a class interval of two starting from 26 weeks and the maximum frequency distribution is seen in the age group 26-28 weeks. In the following table the frequency distribution of male and female neonates also can be seen, maximum being female neonates with an age group of 26-28 weeks.

The premature infants were grouped into Group-1, PMB (Premature neonate without any known complications) and Group-2, PMB+AB (Premature neonate with known complications). The following tables (Table-3), shows the frequency distribution of the neonates and their percentages in correlation with gestational age group.

The lying position of the neonate observed shows 100% babies of age group 26-28 lie in supine resting position, 50% in side lying and 50% are in supine position in age group 29-31, 12.5% in prone position and 87.5% in supine position in age group 32-34, 100% supine in age group 35-37 weeks, 100% supine in 38-40 weeks.

The average heart rate throughout data collection period is shown in table-4. Within the group of PMB, in male neonate the average heart rate 155 bpm whereas female neonate shows an average of 152.3bpm. In PMB+AB group, female average heart rate was 154.4 bpm, whereas in males it was reported as 160.7 bpm.

The average respiratory rate (Male-52, Female -51.41 and total 51.72) is shown in the following table and the percentage of oxygen saturation (Male-96.6%, Female -96.4% and total 96.5%) is shown in the following table with differences in both groups of neonates (Table-4).

The average arousal state of the neonate on non painful stimulus including, simple touch, pressure and temperature is recorded highest as deep sleep(72%).

The status of the preterm neonate with the instrument connected during the intervention as per gestational age group is as follows. (Graph: 2)

The total average pain score taken at different intervals is as follows (table-5). The mean pain score is which is considered as moderate as per PIPP table. The standard deviation is 3.517. The descriptive statistics for the total pain score is given in table-5. The likelihood dispersal of pain is typical.

The averages of hemodynamic changes recorded during the painful stimulus shows the following features such as in Heart rate, Respiratory rate and Breathing pattern (Table- 6.1, 6.2, 6.3). The changes which can't be recorded are not mentioned in the table for calculation. The average alert state score is 1.84 for the babies during the intervention.

DISCUSSION

When it comes to the scenario of recording or measuring of pain, most of the researchers and clinicians had depended the responses of behavioral and physiological aspects which were considered as alternative measures for pain.¹³ Preterm infants are known to show a small magnitude behavioral and physiological responses to acutely painful stimuli, especially when they at younger gestational ages.¹³⁻¹⁶ In addition, preterm infants at earlier gestational ages may display different pain behaviors from those born at later gestational ages¹⁷; therefore, these behaviors may not be captured by pain scales based on pain cues observed in full-term infants. These complexities concluded to recommend a most reliable pain scales for preterm infants must be associated with developmentally pertinent pain indicators¹⁸.

To evaluate the pain processing pattern in preterm neonates at NICU, and to study the hemodynamic changes in response to painful and tactile stimuli, the following study is compared with similar studies which were comprehended by Beatriz Oliveira Valeri et al.¹⁹ Out of the Six studies which we referred, investigated differences in clinical pain responses during the neonatal phase in different genders of the neonates, four studies found no significant sex differences.²⁰⁻²² Only two studies found differences between male and female preterm newborns showing more pronounced pain responses in males than in females.^{23,24}

In a cross-sectional study, Bartocci et al.,²³ found sex differences in infants during a painful venipuncture procedure for blood collection. The male preterm infants had shown a greater response over female preterm neonates born at 28–36 weeks of gestational age. Males expressed a significant increase in bilateral cortical activation compared with females, and they exhibited a left hemisphere dominance.



In a cross-over study, Holsti et al.,²¹ compared two groups of preterm infants with different gestational ages (<30 weeks vs. >30 weeks; gestational age, 24–32 weeks) during sessions of painful (i.e., heel lance) and stressful (i.e., clustered care) procedures. Data collection was done at two levels, clustered care after rest and clustered care after pain. Male neonates exhibited sustained behavioral responses to stress cues into the recovery phase of the clustered care after pain (i.e., the heel lance procedure) which was assessed by the Newborn Individualized Developmental Care and Assessment Program (NIDCAP). Our study has shown that the pain perceptions in preterm neonates of male and female categories are not statistically different.

The present study correlated with the following study by Gibbins et al.,²² less mature showed fewer changes in total facial activity responses from baseline when the blood collection procedure was done. Infants in the early premature group had lower value of oxygen saturation levels. When these researchers had done a comparison of mean oxygen saturation and heart rate differences between baseline value and lance phase values, the 28–31 weeks of gestational age group exhibited the greatest changes which in line with the present study.

Results of the studies of experimental pain showed that the pain threshold is varied according to the gestational age at birth. This also affects the sensitivity to pain in the teenage period. It was shown an association between a lower gestational and lower pain thresholds and higher pain sensitivity. The longitudinal studies of Goffaux et al., and Hermann et al., demonstrated^{25,26} that gestational age is an important factor in physiological pain responses during pain experiences later in childhood. In case of thermal perceptual sensitization, the premature children exhibited higher scores of pain threshold assessments when compared to full-term children. Preterm children at 11 years of age were more sensitive to the identification of thermal changes than full-term children.²⁷ These results highlight the importance of not only comparing children born preterm and full-term but also examining gestational age.

CONCLUSIONS

The pain perception according to the recorded score is moderate in the premature neonates and the perception score is comparatively high in preterm neonates with known abnormalities. The pain perception did not show any statistical difference in male and female preterm neonates. The infants born at 29–31 weeks of gestational age group showed greatest changes in the hemodynamic patterns during exteroceptive painful stimulation. The lowest gestational age group of preterm neonates showed high state of alertness during stimulation.

Tables and Graphs

Table-1: Descriptive statistics of birth weight for neonates.

Table-3: Present wt (in gms/kgs)	
Mean	1.541
Standard Error	0.121697
Median	1.5
Mode	0.85
Standard Deviation	0.608483
Sample Variance	0.370252
Kurtosis	-1.2655
Skewness	0.146925
Range	1.94
Minimum	0.66
Maximum	2.6
Sum	38.525
Count	125
Largest(1)	2.6
Smallest(1)	0.66
Confidence Level(95.0%)	0.25117



Table-2: Frequency distribution of gestational week and sex of the neonate

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Sr No	Age Group	Female	Male	Total
1	26-28	19	16	35
2	29-31	8	4	12
3	32-34	14	14	28
4	35-37	13	16	29
5	38-40	10	11	21
	Total	61	64	125

Table-3 Frequency distribution of preterm neonates

Table-3: Frequency distribution of two groups of preterm neonates			
Age Group	PMB	PMB+AB	Total
26-28	16	19	35
29-31	7	5	12
32-34	15	13	28
35-37	15	14	29
38-40	11	10	21
Total	64	61	125

Table-4: Average respiratory rate, oxygen saturation and heart rate in preterm neonates in comparison with gender

Average respiratory rate				Percentage of oxygen saturation			Average heart rate		
Respiratory Rate	Female	Male	Total	Female	Male	Total	Female	Male	Total Average
PMB	51.62	50.66	51.21	97.1%	96.5%	96.9%	152.3	155.0	153.4
26-28	45.33	46	45.5	97.7%	94.0%	96.8%	144.7	176.0	152.5
29-31	48	42	45	96.0%	100.0%	98.0%	148.0	142.0	145.0
32-34	60	58	59	96.3%	96.3%	96.3%	162.7	156.7	159.7
35-37	49	48	49	99.0%	99.0%	99.0%	148.0	148.0	148.0
38-40	42	42	42	96.0%	96.0%	96.0%	142.0	142.0	142.0
PMB +AB	52.6	52.16	52.36	95.8%	96.3%	96.1%	154.4	160.7	157.8
26-28	44.5	56.33333	51.6	95.5%	97.7%	96.8%	147.0	161.3	155.6
29-31	48	42	45	96.0%	100.0%	98.0%	148.0	142.0	145.0
32-34	85	42	63.5	96.0%	96.0%	96.0%	192.0	148.0	170.0
35-37	44.5	51	47.75	96.0%	94.5%	95.3%	143.0	166.0	154.5
38-40	42	42	42	96.0%	96.0%	96.0%	142.0	142.0	142.0
Total	52	51.41	51.72	96.6%	96.4%	96.5%	153.1	157.8	155.4



Table-5. Descriptive Statistics for Pain Score

Table-5. Descriptive Statistics for Pain Score	
Mean	8.04
Standard Error	0.703515
Median	9
Mode	12
Standard Deviation	3.517575
Sample Variance	12.37333
Kurtosis	-0.69022
Skewness	-0.46684
Range	13
Minimum	1
Maximum	14
Sum	201
Count	125
Largest(1)	14
Smallest(1)	1
Confidence Level(95.0%)	1.451984

Table-6: The averages of hemodynamic changes recorded during the painful stimulus shows the Heart rate, Respiratory rate and Breathing pattern

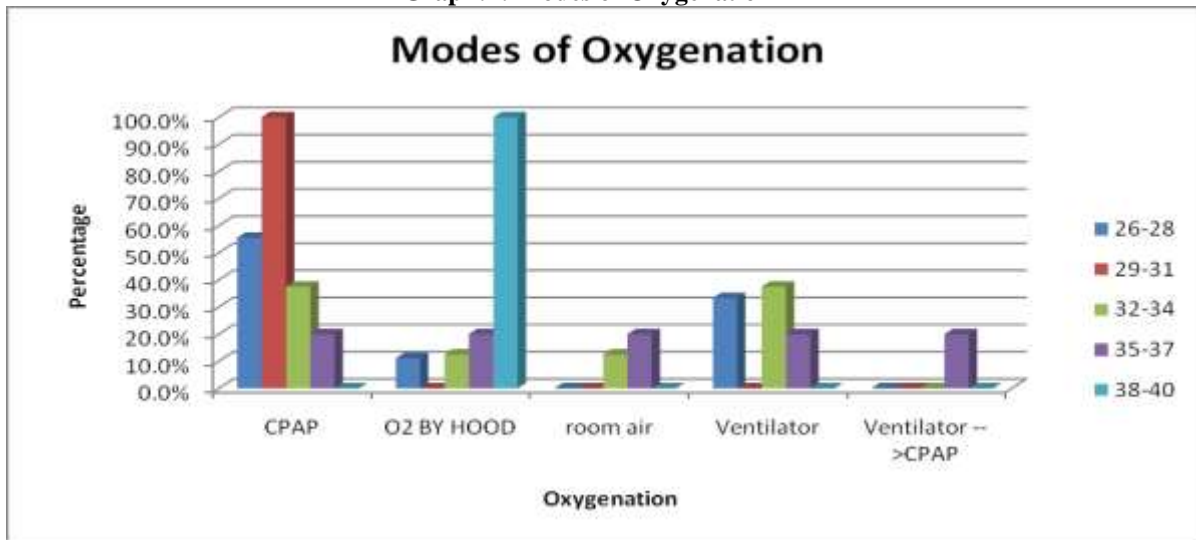
	Maximal heart rate	Breathing status	Maximal oxygen saturation
PMB	0.5	0.5	0.16
26-28	0.25	1.00	0.10
29-31	1.50	0.50	0.14
32-34	0.33	0.64	0.17
35-37	1.20	0.52	0.16
38-40	0.40	1.00	0.14
PMB +AB	1	0.33	0.37
26-28	1.20	0.24	0.32
29-31	1.20	0.33	0.54
32-34	1.00	0.35	0.36
35-37	1.20	0.34	0.35
38-40	1.04	0.35	0.37
Total	0.7	0.4	0.25



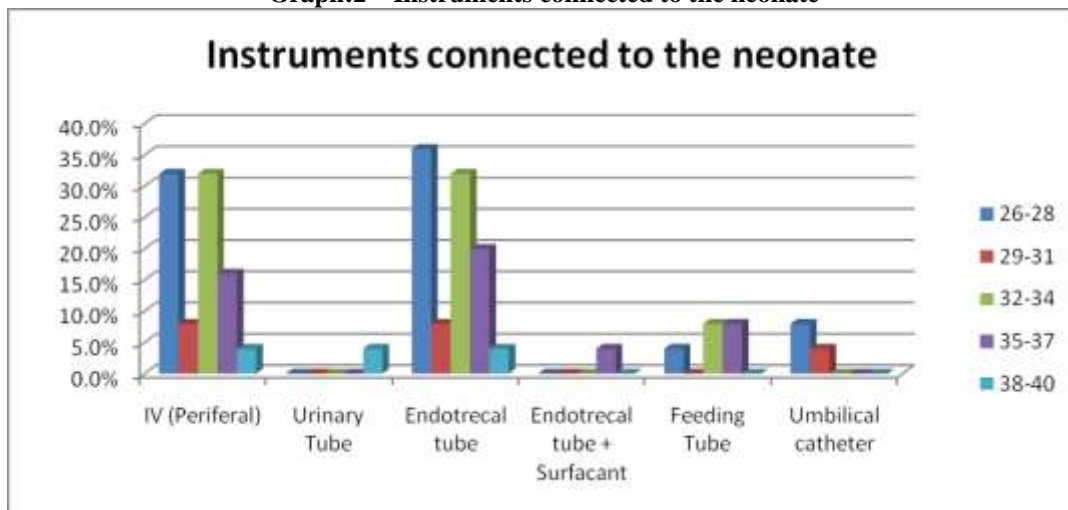
Table-7: Average pain score for different age groups

		Table-12: Average pain score for different age groups				
Age group	PMB			PMB+ AB		
	Female	Male	Total	Female	Male	Total
26-28	9.0	8.0	8.5	11.5	11.0	10.1
29-31	10.0	11.0	10.5	11.0	10.7	10.5
32-34	8.3	9.0	8.5	12.0	4.0	8.5
35-37	3.0	3.3	3.2	5.0	1.5	3.2
38-40	5.1	5.0	5.0	5.0	5.1	5.0
Total	8.1	8.5	8.0	9.0	6.7	8.0

Graph:1: Modes of Oxygenation



Graph:2 – Instruments connected to the neonate





REFERENCES

1. SelvamRamchandran, Sudip Dutta. Early Developmental Care Interventions Of Very Low Birth Weight Infants. *Indian Pediatr.* August 15, 2013; 50: 765-770.
2. Lianne Woodward J, Peter Anderson J, Nicola Austin C, Kelly Howard, Terrie Inder E. Neonatal MRI to Predict Neurodevelopmental Outcomes in Preterm Infants. *N Engl Med.* August 17, 2006.
3. Spence K, Gillies D, Harrison D, Johnston L, Nagy S. A reliable pain assessment tool for clinical assessment in the neonatal intensive care unit. *Journal of Obstetric, Gynecologic, & Neonatal Nursing.* 2005 Jan; 34(1):80-6.
4. McNair C, Ballantyne M, Dionne K, Stephens D, Stevens B. Postoperative pain assessment in the neonatal intensive care unit. *Archives of Disease in Childhood-Fetal and Neonatal Edition.* 2004 Nov 1; 89(6):F537-41.
5. Lundqvist P, Kleberg A, Edberg AK, Larsson BA, Hellström-Westas L, Norman E. Development and psychometric properties of the Swedish ALPS-N eo pain and stress assessment scale for newborn infants. *Acta Paediatrica.* 2014 Aug; 103(8):833-9.
6. Holsti L, Grunau RE, Shany E. Assessing pain in preterm infants in the neonatal intensive care unit: moving to a 'brain-oriented' approach. *Pain management.* 2011 Mar; 1(2):171-9.
7. Cignacco E, Mueller R, Hamers JP, Gessler P. Pain assessment in the neonate using the Bernese Pain Scale for Neonates. *Early human development.* 2004 Jul 1; 78(2):125-31.
8. Jonsdottir, Rakel & Kristjansdottir, Gudrun. (2006). The sensitivity of the premature infant pain profile – PIPP to measure pain in hospitalized neonates. *Journal of evaluation in clinical practice.* 11. 598-605. 10.1111/j.1365-2753.2005.00603.x.
9. Anand KJ, Carr DB: *The Neuroanatomy, Neurophysiology & neurochemistry of pain, stress & analgesia in newborns & children, Pediatr Clin North Am* 36:795-822, 1989.
10. Porter FL, Miller JP, Cole FS, Marshall RE: A Controlled clinical trial of local anesthesia for lumbar punctures in newborns, *Pediatrics* 88:663-669, 1991.
11. Stevens BJ, Gibbins J, Yamada J, Dionne K, Lee G, Johnston C, Taddio A. The premature infant pain profile-revised (PIPP-R): initial validation and feasibility. *The Clinical journal of pain.* 2014 Mar 1; 30(3):238-43.
12. Hudson-Barr D, Capper-Michel B, Lambert S, Palermo TM, Morbeto K, Lombardo S. Validation of the pain assessment in neonates (PAIN) scale with the neonatal infant pain scale (NIPS). *Neonatal Network.* 2002 Oct 1; 21(6):15-21.
13. Grunau RV, Whitfield MF, Petrie JH, Fryer EL. Early pain experience, child and family factors, as precursors of somatization: a prospective study of extremely premature and fullterm children. *Pain.* 1994; 56(3):353-359.
14. Hohmeister J, Demirakca S, Zohsel K, Flor H, Hermann C. Responses to pain in school-aged children with experience in a neonatal intensive care unit: Cognitive aspects and maternal influences. *Eur. J. Pain.* 2009; 13(1):94-101.
15. Rogers CE, Anderson PJ, Thompson DK, et al. Regional cerebral development at term relates to school-age social-emotional development in very preterm children. *J. Am. Acad. Child Adolesc. Psychiatry.* 2012; 51(2):181-191.
16. Miller SP, Vigneron DB, Henry RG, et al. Serial quantitative diffusion tensor MRI of the premature brain: development in newborns with and without injury. *J. Magn. Reson. Imaging.* 2002; 16(6):621-632.
17. Smith GC, Gutovich J, Smyser C, et al. Neonatal intensive care unit stress is associated with brain development in preterm infants. *Ann. Neurol.* 2011; 70(4):541-549.
18. Peterson BS, Vohr B, Staib LH, et al. Regional brain volume abnormalities and long-term cognitive outcome in preterm infants. *JAMA.* 2000; 284(15):1939-1947.
- a. 19. Beatriz Oliveira Valeri; Maria Beatriz Martins Linhares. Pain in preterm infants: effects of sex, gestational age, and neonatal illness severity. *Psychol. Neurosci.* vol.5 no.1.
19. Holsti L, Grunau RE, Whitfield MF, Oberlander TF, Lindh V. Behavioral responses to pain are heightened after clustered care in preterm infants born between 30 and 32 weeks gestational age. *The Clinical journal of pain.* 2006; 22(9):757.
20. Holsti L, Grunau RE, Oberlander TF, Whitfield MF. Specific Newborn Individualized Developmental Care and Assessment Program movements are associated with acute pain in preterm infants in the neonatal intensive care unit. *Pediatrics.* 2004 Jul; 114(1):65-72.
21. Gibbins S, Stevens B, Beyene J, Chan PC, Bagg M, Asztalos E. Pain behaviours in extremely low gestational age infants. *Early human development.* 2008 Jul 1; 84(7):451-8.
22. Bartocci M, Bergqvist LL, Lagercrantz H, Anand KJ. Pain activates cortical areas in the preterm newborn brain. *Pain.* 2006 May 1; 122(1-2):109-17.
23. Holsti L, Grunau RE, Oberlander TF, Whitfield MF. Prior pain induces heightened motor responses during clustered care in preterm infants in the NICU. *Early human development.* 2005 Mar 1; 81(3):293-302.
24. Goffaux P, Lafrenaye S, Morin M, Patural H, Demers G, Marchand S. Preterm births: can neonatal pain alter the development of endogenous gating systems?. *European Journal of Pain.* 2008 Oct 1; 12(7):945-51.
25. Hermann C, Hohmeister J, Demirakca S, Zohsel K, Flor H. Long-term alteration of pain sensitivity in school-aged children with early pain experiences. *Pain.* 2006 Dec 5; 125(3):278-85.
26. Walker SM, Franck LS, Fitzgerald M, Myles J, Stocks J, Marlow N. Long-term impact of neonatal intensive care and surgery on somatosensory perception in children born extremely preterm. *PAIN®.* 2009 Jan 1; 141(1-2):79-87.