The effects of handling on the sleep of preterm infants

O efeito da manipulação sobre o sono do recém-nascido prematuro

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Abstract

Objective: Identify the types of handling procedures performed on preterm infants and assess their influence on total sleep time, wake time and the objective sleep variables.

Methods: Observational and correlational study conducted in the neonatal unit of a teaching hospital. The sample was made up of 12 preterm infants who met the inclusion and exclusion criteria established for the study. Data were collected from March 2013 to April 2014, by means of polysomnography, filming and observation for 24 uninterrupted hours. Descriptive statistics, the Friedman test, Pearson's correlation and linear regression, with significant values of $p \leq 0.05$, were used.

Results: The preterm infants studied were predominantly late preterm, female, with low birth weight, and a mean chronological age of 14 days. The newborns were handled an average of 176.4 ($\pm$37.9) times during a 24-hour period; 58% of the handling procedures were for monitoring. The proportion of total sleep time was 57.2% in 24 hours. There was no statistically significant correlation between frequency and duration of direct and ambient handling and the sleep of preterm infants in a 24-hour period. Single handling procedures had a strong positive correlation with wake time.

Conclusion: Handling was related to monitoring, therapeutic/diagnostic and hygiene/comfort, with a prevalence of direct, single handling procedures. No statistically significant influence on the objective sleep variables was identified, except for single handling procedures where there was a correlation with wake time.

Resumo

Objetivo: Identificar os tipos das manipulações realizadas em recém-nascidos prematuros e avaliar a influência sobre os tempos totais de sono, vigília e as variáveis objetivas do sono.

Métodos: Estudo observacional e de correlação realizado em uma unidade neonatal de hospital universitário. A amostra foi constituída por 12 recém-nascidos prematuros que atenderam aos critérios de inclusão e exclusão estabelecidos para o estudo. Os dados foram coletados no período de março de 2013 à abril de 2014 e obtidos por meio do polissonígrafo, filmagem e observação durante 24 horas, ininterruptas. Utilizou-se a estatística descritiva, teste de *Friedman*, correlação de *Pearson* e regressão linear, com valores significantes $p \leq 0,05$.

Resultados: Os prematuros estudados eram predominantemente tardios, do sexo feminino, com baixo peso ao nascer e idade cronológica média de 14 dias. Os neonatos foram manipulados em média 176,4($\pm$37,9) vezes durante as 24 horas, sendo que 58% das manipulações foram para monitoramento. A proporção do tempo total de sono foi 57,2% em 24 horas. Não houve correlação estatisticamente significante entre as frequências e os tempos de duração das manipulações diretas e do ambiente com o sono dos RNPT em 24 horas. A forma única apresentou correlação fortemente positiva com a vigília.

Conclusão: As manipulações relacionaram-se ao monitoramento, terapêutica/diagnóstica e cuidados de higiene e conforto, com prevalência das manipulações diretas e únicas, não sendo identificada influência estatisticamente significante sobre as variáveis objetivas do sono, com exceção das manipulações únicas que apresentaram correlação com o tempo de vigília.

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Introduction

Scientific and technological advances in the last few decades have provided greater resources for the care and survival of hospitalized preterm infants.[1-4] In modern neonatal intensive care units (NICU), preterm infants are generally subjected to multiple sensory and physical stimuli associated with excessive handling by health teams.

Most of the time, the care given to hospitalized preterm infants is based on routines established by the department and not on the needs manifested by the newborn at the time. Consequently, the care provided by health teams can trigger important changes in the organisms of preterm infants, such as in the sleep-wake cycle, resulting in sleep fragmentation and even its deprivation, which can lead to significant changes in the development of preterm infants, especially sensorineural.[5] The immature nervous system of preterm infants is unable to properly process stimuli such as those resulting from the frequent handling to which they are normally exposed during hospitalization.[6-8]

A study conducted in an NICU in a university hospital in New Zealand, which assessed handling procedures performed by the health team, found that the newborns were handled an average of 234 times in 24 hours, concluding that handling had been excessive.[9]

A descriptive, observational study conducted in a neonatal intensive care unit to examine the handling of 20 hospitalized preterm infants found that they were handled 768 times and subjected to 1,341 procedures over the course of 14 days. In 24 hours, total handling time was 2 hours and 26 minutes on average. It was concluded that the preterm infants were handled excessively and that most handling occurred in an isolated form, lasting less than a minute.[10]

It is well-known that the excessive handling that newborns undergo is sometimes painful and triggers physiological changes that affect their recovery. This fact was reported in a cross-sectional study whose objective was to assess pain in 34 newborns hospitalized in a neonatal unit. The most painful procedures experienced by the newborns were orotracheal intubation and intravenous catheter insertion. It was concluded that pain should be evaluated when performing handling procedures, especially in preterm infants, since their central nervous system is immature and painful sensations can lead to changes in physiological parameters, future pain perception, and the sleep-rest cycle, among others.[11]

The analysis of the polysomnograms and images obtained by filming 25 newborns, to diagnose brain dysfunction and assess the influence of handling on sleep and ventilatory stability, found that the newborns studied were handled during all sleep stages. In 57% of the handling procedure, awakening occurred, and apnea was identified in 19.5% of the preterm infants. This indicates a direct relationship between handling frequency and sleep and respiratory events.[12]

Studies have found that excessive handling and sleep deprivation in preterm infants may impair neuromotor development, induce hyperexcitability, trigger or exacerbate psychiatric diseases, and cause excessive daytime sleepiness.[1,13-15] Furthermore, sleep is the main behavioral state of preterm infants and constitutes an important basic need. It is conducive to maturation of the central nervous system, memory consolidation, learning, energy maintenance, thermoregulation, promotion of protein synthesis, and the production of certain hormones, such as growth, thyroid stimulation, melatonin, prolactin, renin, and cortisol.[14-17]

Sleep disturbance at the onset of life, besides causing newborns discomfort, can also result in future changes related to cognition, attention, increased risk of asthmatic diseases, obesity, anxiety, depression, and behavioral and social impairment.[18]

The sleep of newborns is polyphasic and ultradian, with an average duration of 16 to 18 hours per day, which corresponds to approximately 70% of the 24 hours. The need for sleep of preterm infants varies according to their development stage and individual physiological characteristics.[1,18-19]

Sleep during the neonatal period is divided into three stages: Active sleep (AS) or REM, in which the newborn manifests rapid eye movement, high physiological activity, and irregular heartbeats and breathing, with a strong correlation with brain growth.[20] The other stage is called quiet sleep (QS) or NREM (non-rapid eye movement), which is characterized by slower waves when recorded in electroencephalograms (EEG). During this stage, cell regeneration, protein synthesis and release of hormones, such as insulin, melatonin, and growth, occur.[21,22] The third stage is called indeterminate sleep (IS), typified by the non-manifestation of characteristics of the quiet and active sleep stages, clearly defined in EEG.[22]

Due to the inherent characteristics of premature infants who require various types of care associated with large amounts of handling in the hospital environment, the present study sought to identify the handling procedures and assess their influence on total sleep time, wake time and the objective sleep variables of hospitalized premature infants.

Methods

This was a descriptive, correlational study conducted in an intermediate neonatal care unit in a university hospital in the city of São Paulo, with 16 beds distributed among four rooms: two for intensive care and the rest for step-down care. Newborn care was provided by a multidisciplinary team that generally had the collaboration of professors and students from undergraduate and graduate courses from various fields of knowledge. In the routines implemented in the health service, the parents of newborns could remain with their infant during hospitalization. It should be noted that only a few care strategies focused on newborn development were adopted in the care provided to newborns.

The sample was made up of 12 premature infants. The inclusion criteria were: premature infant receiving care in an incubator; heart rate, respiratory rate and body temperature within ranges of normality; weight between 1,200 and 2,000 grams; and positive transient-evoked otoacoustic emission test (TEOAE). Preterm infants were excluded for the following reasons: use of phototherapy treatment; invasive or non-invasive mechanical pulmonary ventilation; diagnosis of intraventricular hemorrhage Grades II, III and IV; use of corticosteroids or CNS depressants in the last 24 hours; and mothers with a history of illicit drug use during pregnancy.

Variables were selected to characterize the preterm infants and their handling, as well as the sleep stages, called objective sleep variables.

The variables related to handling were obtained through a Sony DCR-PJ25 camcorder (Manaus, Brazil) fastened to a stainless steel support. The camera was focused on the center of the incubator, so as to view only the preterm infant and the procedures performed inside the incubator. The audio function of the camcorder was disabled in compliance with ethical aspects. The images produced by the camcorder were analyzed by three nurses who worked in neonatology, in order to identify the handling procedures and register them on an electronic spreadsheet. Thirty-nine procedures were identified that were categorized by seven experts: four nurses that provided newborn care and three nurses from the academic sphere. The procedures were grouped into the categories of monitoring, therapeutic/diagnostic, hygiene/comfort and feeding. The agreement analysis among raters produced values greater than or equal to 0.7, according to Cronbach's alpha coefficient, indicating satisfactory consensus.

The variables in reference to handling were classified as: occurrence (yes or no), frequency (number of times the newborn was touched), form (single or multiple procedures), type (monitoring, therapeutic/diagnostic, hygiene/comfort and feeding) and time (duration of the direct or indirect/ambient handling). Direct handling was defined as contact of the agent with the skin or any device attached to the newborn. Indirect/ambient handling referred to handling of the microenvironment of the incubator, such as when the hatches were opened, with no contact with the skin or any device connected to the preterm infant.

The sleep-related variables referred to total sleep time, defined by adding up the time in minutes of active, quiet and indeterminate sleep, in addition to as AS time, QS time and wake time. They were obtained from a polysomnograph - model Alice 5- Respironics® (Royal Philips, Holland) - which was installed by a professional from the Sleep Institute of the Federal University of São Paulo/UNIFESP and the Research Support Fund Association (AFIP), and attached for 24 uninterrupted hours. The polysomnograms were interpreted by a neuropediatrician specialized in sleep, in accordance with the sleep study guidelines recommended by the American Academy of Sleep Medicine, version 2.1.[23]

The data was collected from March 2013 to April 2014, after approval from the institution's Research Ethics Committee [CEP No. 19387] and after the Free and Informed Consent Forms were signed by the people responsible for the infants.

The data collected was entered on Excel® Microsoft for Windows spreadsheets, and at the end of the collection, underwent a statistical analysis with SPSS 17.0 for Windows software, using means, medians, standard deviation and minimum and maximum values. To compare the proportions of duration and frequency of handling procedures in the different periods of the day, the nonparametric Friedman test was used, since the measurements were performed on the same individuals. Pearson correlation coefficient analysis was used to assess the correlation between frequency and duration of direct and ambient handling and sleep times for each period in 24 hours. For sleep time and handling procedures, linear regression analysis was used, considering $p \leq 0.05$ as significant values.

Results

The sample was comprised of predominantly female preterm infants, classified as late preterm, with low birth weight and 14 days of life on average, at the time of the data collection. The newborns had good vitality at birth, with an Ap-gar score at the 1st and 5th minutes greater than or equal to seven. In terms of the variables related to handling frequency of preterm infants, there were 2,117 handling procedures during 24 hours, with a mean of 176.4 (±37.9) handling procedures per newborn in the period investigated. Table 1 presents the variables related to handling of preterm infants.

Table 1. Handling according to type, duration, and form, during the 24-hour assessment (n=2117)

Variables	n (%)	Mean ±SD (Min-Max)
Type		
Direct handling	1546(73)	73.9±15.7(56-104)
Ambient handling	571(26.9)	47.6±13.7(30-74)
Duration (minutes)		
Direct handling	2,880.9(76.4)	228.3±78.6(140.4-371.2)
Ambient handling	892.6(23.6)	76.3 ±51.1(29.6-183.9)
Form		
Single	550(61.4)	45.8±15.236(26.0-75.0)
Grouped	346(38.6)	28.8±5.7(23.0-41.0)

SD - standard deviation; Min - minimum value; Max - maximum value

Higher frequencies of direct handling and consequent longer mean duration were noted, with a predominance of them being single procedures. The direct handling procedures distributed among the four categories are presented in table 2. The distribution of the handling procedures, according to category in the four periods of the day, was assessed with the Friedman test.

Regarding the classification of the handling procedures, according to the primary data there was a higher occurrence in the monitoring category, followed by handling procedures related to the hygiene/comfort of the preterm infant (activities not limited to hospital care). It can be inferred that the results in reference to monitoring may be associated with the need for repositioning the electrodes on the newborns for adequate recording of data by the polysomnography (548; 64.3%). In the therapeutic/diagnostic category, administration of drugs via gastric tube was predominant (17; 37.8%); in the hygiene and comfort category, handling procedures for change of position were prevalent (95; 20.8%), and in relation to feeding, administration by enteral tube had the highest frequency (85; 45.9%). In terms

of handling for therapeutic/diagnostic purposes, there was a statistically significant difference in frequency during the periods of the day, where it was higher in the morning period (p<0.01).

Table 3 presents the time analysis for total sleep, wake time and the stages of active, quiet and indeterminate sleep, in minutes, in 24 hours and in the different periods of the day analyzed. The Friedman test was used to assess the distribution of the sleep-related variables in the four periods of the day.

The total sleep time mean for preterm infants in 24 hours was 824.3 (±237.03) minutes which corresponds to 57.2% of the day, i.e., 13.7 hours. As for the objective sleep variables, there was a homogeneous distribution in the four periods of the day, with a predominance of quiet sleep.

Table 4 presents the correlation between type, frequency, and duration of handling procedures and the time variables of total sleep, wake time and their respective stages.

Table 2. Direct handling procedures performed in 24 hours and in the periods of the day on preterm infants, according to categorization (n=1546)

Direct handling	24 hours Mean±SD (Min-Max)	Morning Mean±SD (Min-Max)	Afternoon Mean±SD (Min-Max)	Night 1 Mean±SD (Min-Max)	Night 2 Mean±SD (Min-Max)	*p-value
Monitoring	71±20.75	17.67±7.54	19.25±8.04	14.9±6.7	19.1±11.9	0.23
(n=852)	(46-113)	(7-31)	(6-30)	(2-26)	(6-48)	
Therapeutic/diagnostic	3.75±2.42	1.92±1.08	0.75±0.97	0.75±1.2	0.2±0.6	<0.01
(n=45)	(0-8)	(0-4)	(0-2)	(0-4)	(0-4)	
Hygiene/comfort	38.67±21.05	12.08±8.67	10.92±4.89	7.5±4.7	8.1±9.3	0.27
(n=464)	(14-81)	(0-27)	(5-20)	(2-16)	(0-33)	
Feeding	15.42±6.69	3.92±1.62	3.50±1.57	3.9±2.6	4.0±3.0	0.63
(n=185)	(6-26)	(2-7)	(1-6)	(0-10)	(1-8)	

Min - minimum value; Max - maximum value; SD - standard deviation; *p - Friedman test

Table 3. Total sleep time, wake time and the stages of active, quiet and indeterminate sleep, in minutes, in 24 hours and in the periods of the day

Variables	24 hours Mean±SD (Min-Max)	Morning Mean±SD (Min-Max)	Afternoon Mean±SD (Min-Max)	Night 1 Mean±SD (Min-Max)	Night 2 Mean±SD (Min-Max)	*p-value
Total sleep time	824.33±237.03 (100-1000)	220.96±36.07 (169-275)	225.17±35.18 (158-301)	230.29±29.06 (167-280)	219.08±43.63 (159-287)	0.06
AS Time	279.63±57.37 (213-364)	75.75±34.79 (39-157)	76.25±27.73 (35-119)	61.50±33.23 (16-123)	69.29±18.00 (31-102)	0.83
QS Time	348.63±89.43 (244-507)	83.54±35.02 (42-164)	88.63±31.29 (40-137)	95.50±31.57 (31-154)	80.00±30.61 (29-128)	0.84
IS Time	271.92±46.28 (186-364)	61.67±15.41 (39-87)	64.08±15.10 (48-93)	73.29±14.94 (46-98)	69.79±18.00 (31-102)	0.73
Wake time	578.46±94.36 (94.3-440)	139.04±36.07 (85-191)	135.17±34.96 (59-203)	129.71±29.06 (80-194)	140.83±43.74 (73-202)	0.99

AS - Active Sleep; QS - Quiet Sleep; IS - Indeterminate Sleep; Min - minimum value; Max - maximum value; SD - standard deviation; *p - Friedman test

Table 4. Correlation between type, duration and frequency of handling procedures and total sleep time (TST), active sleep (AS), quiet sleep (QS), indeterminate sleep (IS) and wake time, in minutes, over a 24-hour period

Variables (24 hours)	TST r(*p-value)	AS r(*p-value)	QS r(*p-value)	IS r(*p-value)	Wake time r(*p-value)
Type					
Single	-0.025(0.939)	0.113(0.727)	-0.439(0.154)	0.156(0.628)	0.616(0.033)
Grouped	0.064(0.843)	0.263(0.409)	0.120(0.710)	-0.198(0.537)	-0.174(0.589)
Duration					
Direct	0.355(0.257)	-0.162(0.615)	0.071(0.827)	-0.104(0.748)	-0.218(0.495)
Ambient	0.265(0.406)	0.297(0.349)	0.009(0.977)	-0.485(0.110)	-0.246(0.441)
Frequency					
Direct	0.158(0.623)	0.266(0.403)	-0.476(0.117)	0.071(0.826)	0.482(0.113)
Ambient	0.226(0.479)	-0.318(0.313)	0.253(0.427)	-0.025(0.940)	-0.179(0.578)

AS - Active Sleep; QS - Quiet Sleep; IS - Indeterminate Sleep; *p-value - Pearson correlation test

There was no statistically significant correlation between frequency and duration of direct and ambient handling and the sleep of preterm infants in 24 hours. This suggests that the handling-related variables did not influence sleep. In terms of total wake time, no statistically significant correlation was found between frequency and duration of handling procedures, except for the single procedure form where there was a strongly positive correlation with wake time.

Discussion

Assessment of the handling of hospitalized preterm infants and its influence on sleep in a 24-hour period enabled identifying a higher frequency and duration of single and direct handling procedures, which may explain the longer total wake time and, consequently, the lower total sleep time. The use of polysomnography, which is considered the most reliable method for sleep assessment,[24] influenced the increased number of handling procedures due to the need to reposition the electrodes.

In the present study, the results showed that preterm infants were handled around 20% of the total time recorded. This finding corroborates a similar study conducted in a neonatal unit which used filming to record the handling of newborns. It was noted that, in a 24-hour period, the preterm infants were subjected to some form of handling 18% of the time.[10] In light of the results obtained, it is important to establish care routines, since, among other factors, excessive handling can trigger pain, especially in preterm infants who have low capacity to release catecholamines, which can negatively affect the development of the CNS.[25,26]

In the analysis of the occurrence of handling of preterm infants, according to periods of the day, the distribution was similar to the four times investigated in the present study, with the exception of direct handling for therapeutic/diagnostic purposes, where frequency was higher in the morning period. These results indicate an urgent need to implement individualized care routines, based on strategies for grouping handling procedures and assessing behav-

ioral and clinical signs in newborns, in order to respect and promote the sleep-wake cycle.[27]

To the best of their knowledge, the authors did not find any studies in the literature that addressed the association between handling of preterm infants and polysomnographic sleep assessment over a 24-hour period, which makes the present study unique.

The results demonstrated that newborn handling did not significantly influence sleep during the 24-hour period. It could be hypothesized that the results obtained are associated with the phenomenon of newborn adaptation, which is characterized by reduced behavioral response to repeated and frequent stimuli, since preterm infants were studied, with a chronological age of 14 days, and who were therefore submitted to numerous handling procedures during hospitalization.[28]

The positive correlation between single handling procedures and total wake time enabled inferring that the stimuli resulting from these handling procedures may have caused more awakenings and sleep fragmentation, leading to increased total wake time. This finding is very similar to another study in which it was noted that in a 4-month period of hospitalization, preterm infants were handled 82 to 142 times a day by nurses, which created periods from 4.6 to 9.2 minutes of uninterrupted sleep.[26] A study conducted in an NICU of a children's hospital in São Paulo, with 9 preterm infants evaluated in 6-hour periods over 17 consecutive days, concluded that preterm infants were handled 45.4 times on average, with a total mean duration of 5.6 hours, suggesting that the time allotted for sleep and rest was insufficient.[17]

To minimize the harmful effects of the environment and excessive handling on the development of preterm infants, it is proposed that interventions be based on individualized care through observing the behavior of the newborn before, during and after each procedure, in addition to grouping the activities, in order to minimize the number of single handling procedures and promote an adequate environment for the development of preterm infants and the establishment of sleep-wake cycles.[5,10,29-30]

The preterm infants who were examined slept approximately 57.2% of the 24-hour period, diverg-

ing from the literature which indicated that preterm infants, at different gestational ages, had an average of 16 to 18 hours of sleep, corresponding to approximately 70% of 24 hours.[2,31,32] The preterm infants experienced sleep deprivation, even without identification of the influence of handling procedures. Therefore, the harmful effects of deprivation, such as impaired development, especially sensorineural, weight gain, length of hospital stay and irritability, among others, should be considered.[31-32]

The preterm infants remained, on average, more time in QS, followed by AS and IS, contrary to a study that reported the predominance of AS, during approximately 80% of the total time, mainly in preterm infants with lower gestational ages. Studies have found that as newborns mature neurologically, there is an increase in the proportion of AS,[22,31] which matches the results of the present study, since the preterm infants studied were late preterm.

The limitations of the present study were sample size and the presence of ambient stimuli in the unit and inside the incubators that could not be controlled. Thus, it was not possible to disassociate the influence they may have had on lower total sleep time. In addition, the long length of time the polysomnograph remained on the preterm infants constituted a limitation, due to the need to reposition the electrodes on the newborns for accurate data recording.

Conclusion

The handling of preterm infants was predominantly related to monitoring, therapeutic/diagnostic and hygiene/comfort activities, with a prevalence of direct and single handling procedures. No statistically significant influence on total sleep time or on active, quiet or indeterminate sleep was identified. Single handling procedures had a strongly positive correlation with wake time. In summary, the results of the study reinforce the importance of care that focuses on the behavioral signs of preterm infants and the grouping of activities, in order to provide an environment conducive to the sleep-wake cycle and adequate development of preterm infants that require hospitalization in neonatal units.

Collaborations

Maki MT, Orsi KCSC, Tsunemi MH, Padrella-Halliman M, Pinheiro EM and Avelar AFM contributed to the study design, data analysis, relevant critical review of its intellectual content, and approval of the final version for publication.

References

1. Calciolari G, Montirosso R. The sleep protection in the preterm infants. J Matern Fetal Neonatal Med. 2011; 24(1):12-4.

2. Grecco GM, Tsunemi MH, Balieiro MM, Kakehashi TY, Pinheiro EM. Repercussion of noise in the neonatal intensive care unit. Acta Paul Enferm. 2013; 17(6):741-9.

3. O'shea TM. Monitoring developmental outcome of very low birth weight J Pediatr (Rio J). 2012; 88(6):452-4.

4. Magalhães FJ, Lima FE, Rolins KM, Cardoso MV, Scherlocks SM, Albuquerque LS. Physiological responses andbehaviorof neonatal handling in neonatal intensive care unit. Rev Rene. 2011; 12(1):136-43.

5. Gaíva MA, Marquesi MC, Rosa MK. O sono do recém-nascido internado em unidade de terapia intensiva:cuidados de enfermagem. Ciênc Cuid Saúde. 2010; 9(3):602-9.

6. Machado RN, Winograd M. The importance of tactile experiences in the psychic formation. Estud Pesq Psicol UERJ. 2007; 7(3): 426-76.

7. Martins CP, Tapia CE. [The skin of the premature newborn under the nurse's evaluation:orientating the manteinance of cutaneous integrity]. Rev Bras Enferm. 2009; 62(5):778-83. Portuguese.

8. Badr LK. Pain interventions in premature infants: what is conclusive evidence and what is not. Newborn Infant Nurs Rev. 2012; 12(3):141-53.

9. Murdoch DR, Darlon BA. Handling during neonatal intensive care. Arch Dis Child. 1984; 59(10):957-61.

10. Goes FS, Fonseca LM, Scochi CG, Castral TC, Leite AM. Handling of preterm infants in a neonatal intensive care unit. Rev Esc Enferm USP. 2013; 47(6):1272-8.

11. Cruz CT Gomes JS, Kiechner RM, Stumm EM. Evaluation of pain of neonates during invasive procedures in intensive care. Rev Dor. 2016; 17(3):197-200.

12. Levy J, Hassan F, Plegue MA, Sokoloff MD, Kushwaha JS, Chervin RD, et al. Impact of hands-on care on infant sleep in the neonatal intensive care unit. Pediatr Pulmonol. 2017; 52(1):84-90.

13. Brasil. Ministério da Saúde. Manual Técnico: Método Canguru. 2nd ed. Brasília (DF): Ministério da Saúde; 2011. [citado 2017 Out 25]. Disponível em : http://bvsms.saude.gov.br/bvs/publicacoes/metodo_canguru_manual_tecnico_2ed.pdf.

14. Ferreira AM, Bergamasco NH. Behavioral analysis of preterm neonates included in a tactile and kinesthetic stimulation program during. Rev Bras Fisioter. 2010; 14(2):141-8.

15. Rugolo LM. Importance of neurodevelopment monitoring in preterm newborn infants. Rev Paul Pediatr. 2012; 30(4):460-1.

16. Sousa MW, Silva RW, Araújo SA. Quantification of manipulations in neonatal intensive care unit: proposal of protocol elaboration. ConScient Saúde. 2008; 7(2):269-74.

17. Santos JS. Aspectos motores, de comunicação, sono-vigília e melatonina na paralisia cerebral [tese]. [Internet]. Marília (SP): Universidade Estadual Paulista "Júlio de Mesquita Filho"; 2017. [citado 2017 Out 25]. Disponível em: https://repositorio.unesp.br/handle/11449/150800.

18. Costa PF, Galvão J, Pessoa V, Júnior D, Tristão DC, Grossawasser RM. NIDCAP and maturity of sleep of infant born preterms: solution to NICU? Rev Saúde Ciênc Online. 2010; 1(2):101-5.

19. Nunes ML. Sleep disorders. J Pediatr. 2002; 78(Supl 1):S63-72.

20. Bueno C, Wey D.Genesis and ontogenesis of sleep/wake rhythm in humans. Rev Biol. 2012; 9(3):62-7.

21. Parmelee, AH, Stern E. Sleep and the maturing nervous system In: Clemente CD, Purpura DP, Mayer FE, editors. Development of states in infants. New York; Academic Press; 1972. p.199.

22. Hoppenbrouwers T, Hodgman JE, Rybine D, Fabrikant G, CorwinM,Crowell D. Sleep architecture in term and preterm infants beyond the neonatal period: the influence of gestational age, steroids and ventilator support. Sleep. 2005; 28(11):1428-36.

23. Iber C, Ancoli-Israel S, Chesson A, Quan SF. The New Sleep Scoring Manual - The Evidence Behind The Rules. J Clin Sleep Med. 2007; 3(2):107.

24. Brasil. Ministério da Saúde. Secretaria de Estado da Saúde. Manual de neonatologia [Internet]. São Paulo: Ministério da Saeude; 2015. [citado 2017 Out 25]. Disponível em : http://www.saude.sp.gov.br/resources/ses/perfil/gestor/homepage/programa-de-fortalecimento-da-gestao-da-saude-no-estado-de-sao-paulo/consultas-publicas/manual_de_neonatologia.pdf.

25. Guimarães GM. [Polyssomnographic diagnosis[. Pulmão (RJ). 2010; 19(3-4):88-92. Portuguese.

26. Gomes CA, Hahn GV. Manipulação do recém-nascido internado em UTI: Alerta à enfermagem. Destaques Acad. 2011; 3(3):113-22.

27. Formiga CK, Linhares MB. Assesment of preterm children´s early development Rev Esc Enferm USP. 2009; 43(2):472-80. Portuguese.

28. Brasil. Ministério da Saúde. Secretaria de Políticas da Saúde. Área da saúde da criança. Atenção humanizada ao recém-nascido de baixo peso: método Mãe-Canguru. Brasília (DF): Ministério da Saúde; 2002.

29. Bonan KC, Pimentel JF, Tristão RM, Jesus JA, Campos JD. Sleep deprivation, pain and prematurity: a review study. Arq Neuro Psiquiatr. 2015; 73(2):147-54.

30. Als H, McAnulty GB. The newborn individualized developmental care and assessment program (NIDCAP) with kangaroo mother care (KMC): comprehensive care for preterm infants. Curr Womens Health Rev. 2011; 7(3):288-301.

31. Raineki C, Lucion AB, Weinberg J. Neonatal handling: an over view of the positive and negative effects. Dev Psychobiol. 2014; 8(56):1613-25.

32. Graven SN, Browne JV. Sleep and brain development: the critical role of sleep in fetal and early neonatal brain development. Newborn Infant Nurs Rev. 2008; 8(4):173-9.