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ORIGINAL ARTICLE

Longitudinal study of sleep behavior and motor development in low-birth-weight preterm children from infancy to preschool years☆,☆☆

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Abstract
Objective: To verify the relationship between sleep characteristics and motor development in low-birth-weight preterm infants during infancy and preschool years.
Method: Forty-one healthy preterm infants (<37 weeks' gestation) with low birth weight (≤1500 g) were assessed longitudinally at three different time points: at 6 months of corrected age, at 12 months of corrected age, and at 4−5 years of chronological age. At 6 and 12 months, motor development was assessed using the Denver Developmental Screening Test II and Alberta Infant Motor Scale, while sleep-related habits and disturbances were assessed using the Brief Infant Sleep Questionnaire. At 4−5 years, motor development was reassessed using the Pediatric Evaluation of Disability Inventory and sleep was reassessed using the Sleep Disturbance Scale for Children. Correlations were performed using sleep quality as the predictor variable and motor development as the outcome variable.
Results: Most infants had suspected delay/atypical development at 6 and 12 months, with no difference between the scales (p = 1.000). Suspected delay/atypical development were associated with lateral sleep position (p = 0.004), greater number of nighttime awakenings (p = 0.008), and longer awake periods (p = 0.014) only at 6 months. At 4−5 years, the suspected delay/atypical development observed at 6 and 12 months disappeared.

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Conclusions: Sleep quality correlated with delayed/atypical motor development in healthy preterm infants with low birth weight only at 6 months of corrected age, which did not appear to affect later development of motor skills.

Introduction

Improvements in neonatal intensive care have led to a substantial increase in the survival of preterm infants. Currently, approximately 85% of infants with birth weight <1500 g survive.[1] There is evidence of a continuum of outcomes, with each additional week of gestation conferring a survival benefit while reducing the length of initial hospitalization.[2] However, several studies have found that the increase in survival has not been accompanied by a decrease in morbidity.[3–5]

Motor skills are also affected in preterm infants with low birth weight.[6] Edwards et al.[7] showed a significant increase in the risk of motor impairment in infants born at <32 weeks' gestation and/or weighing ≤1500 g compared with term infants. In a literature review, Moreira et al.[8] concluded that preterm infants are more susceptible to motor development, behavior, and school performance abnormalities than children born at term. The pattern and characteristics of sleep in preterm infants have also been suggested as a risk indicator for the development of functional and cognitive impairment.[3] However, despite individual differences in sleep-related behavior between preterm and term infants at birth, after 1 year of age the disparity is no longer apparent.[9,10]

Studies have shown that adequate sleep is essential for optimal infant development, especially during the early development phases.[11] A prospective longitudinal study of sleep and motor development in term infants from 5 to 11 months of age revealed a link between locomotion progress and changes in sleep-wake regulation.[12] However, to date, little is known about the association between sleep quality and motor development in preterm infants.

The present study was therefore designed to examine longitudinally whether sleep characteristics of preterm infants with low birth weight affect motor development during infancy and preschool years. We tested the hypothesis that sleep disturbances would correlate with delayed motor development at 6 and 12 months of age, also affecting later development at 4–5 years of age.

Methods

This longitudinal study was conducted at Hospital São Lucas, a tertiary care teaching hospital in Porto Alegre, southern Brazil, after approval by the institutional research ethics committee (approval no. 11/05327). The research was conducted in accordance with the American Psychological Association ethical standards in the treatment of the study sample. Written parental consent was obtained from all participants prior to inclusion in the study.

Participants

Preterm infants were recruited from the neonatal intensive care unit (NICU) of the hospital from March 2, 2011 to July 12, 2012. The study group consisted of 41 preterm infants (born at <37 weeks' gestation) with low birth weight (≤1500 g) who were assessed longitudinally at three different time points: at 6 months of corrected age, at 12 months of corrected age, and at 4–5 years of chronological age. Exclusion criteria were serious clinical complications preventing participation in any stage of the study, neurological complications, death, or impossibility of reaching the family via telephone or at home after discharge.

Procedure

All infants were recruited on NICU admission. Parents of preterm infants who had been admitted to the NICU were approached by the researchers, informed of the purpose of the study and invited to participate, being assured that participation was voluntary and confidential. Information on neonatal variables and morbidities, birth weight, and birth length were collected from the child's health records filled in at birth.

All instruments were explained and administered to the child's parents by the same researcher trained in child assessment. The researcher remained available for any necessary clarification while the parents were completing the questionnaires. Evaluations at 6 and 12 months of corrected age were performed in an outpatient clinic. At 4–5 years of chronological age, parents were contacted via telephone to schedule home or school visits for evaluation.

Measures

Assessment of infant motor development

At 6 and 12 months of corrected age, parents completed the Denver Developmental Screening Test II (Denver II)[13] and the Alberta Infant Motor Scale (AIMS).[14] A validated Brazilian version of the Denver II was used,[15] consisting of 125 items divided into 4 general areas of development (personal-social, fine motor-adaptive, language, and gross motor). The items were rated as follows: (P) - pass, parent reports that the child does the item; (F) - fail, parent reports that the child does not do the item; and (NO) - no opportunity, the child has not had the chance to perform the item because of restrictions from the parents or other reasons. Results were dichotomized into presence or absence of atypical development. A validated Brazilian version of the AIMS was used,[16] consisting of 58 items measuring spontaneous movements that reflect the quality of weight-bearing, posture, and antigravity skills in prone, supine, sitting, and standing positions. The items were rated as 0 = not observed or 1 = observed, where the lowest and the highest observed items in each position create a window of motor development. Results were dichotomized into presence or absence of suspected delay in motor development.

Between 4 and 5 years of chronological age, motor development was assessed using the Pediatric Evaluation of Disability Inventory (PEDI).[17] A validated Brazilian version of the PEDI was used.[18] Only Part I (Functional Skills) was administered, consisting of 197 items rated 0–1 for performance capability. The final scores were adjusted for age. Adjusted scores between 30 and 70 were considered within the normal range, while scores below 30 indicated delay in motor development.

Assessment of infant sleep

At 6 and 12 months of corrected age, parents completed the Brief Infant Sleep Questionnaire (BISQ).[19] A validated Brazilian version of the BISQ was used,[20] and the following criteria were used to define poor sleepers: (a) the infant wakes >3 times per night; (b) nocturnal wakefulness period is >1 h; or (c) the total sleep time is <9 h.

Between 4 and 5 years of chronological age, sleep was assessed using the Sleep Disturbance Scale for Children (SDSC).[21] A validated Brazilian version of the SDSC was used,[22] consisting of 26 items to assess sleep behavior and disturbances during the previous 6 months. Responses were given on a 5-point Likert scale, where 1 = never, 2 = occasionally (once or twice per month or less), 3 = sometimes (once or twice per week), 4 = often (3 or 5 times per week), and 5 = always (daily). A total score above 39 indicated the presence of sleep disturbances.

Sample size

The sample size was calculated using WinPEPI, version 11.43. Due to the paucity of data in the literature, sample size calculation was based on a pilot study of 15 children. For a significant association between motor development and sleep scores (quantitative variables), we calculated that a sample size of at least 38 preterm infants was necessary to give 90% power to obtain a minimum correlation coefficient of 0.5 between the two variables with 5% significance.

Statistical analysis

Categorical variables were expressed as counts and percentages, and quantitative variables were expressed as mean and standard deviation or median and interquartile range (25th–75th percentile). The Wilcoxon test and McNemar test were used to compare motor development between 6 and 12 months of corrected age. Agreement between AIMS and Denver II scores was assessed using kappa coefficient (κ), where: <0.20 = poor agreement; 0.21–0.40 = fair agreement; 0.41–0.60 = moderate agreement; 0.61–0.80 = good agreement; and >0.80 = very good agreement. Student's *t* test for paired samples was used to compare sleep characteristics between 6 and 12 months of corrected age. Pearson or Spearman coefficients were calculated to test the correlation between quantitative ordinal variables at 6 and 12 months of corrected age and at 4–5 years of chronological age. Pearson's chi-square test or Fisher's exact test were used to test the association between categorical variables, while Student's *t* test for independent samples or the Mann-Whitney test were used for continuous variables. The predictor variable was sleep quality of preterm infants at 6 and 12 months of corrected age according to BISQ scores and at 4–5 years of chronological age according to SDSC scores. Outcome variables were motor development at 6 and 12 months according to AIMS and Denver II scores and at 4–5 years according to PEDI scores. Data were analyzed using SPSS, version 21.0. The significance level was set at $p \leq 0.05$ for all analyses.

Table 1 Neonatal characteristics of preterm infants.

Variable	n = 41
Birth weight (g) – mean ± SD	1196 ± 237
Gestational age (weeks) – mean ± SD	30.7 ± 2.4
1-minute Apgar score – median (P25–P75)	7 (3–8)
5-minute Apgar score – median (P25–P75)	8 (7–9)
No. of prenatal visits – median (P25–P75)	4 (2–7)
Mode of delivery – n (%)	
Vaginal delivery	10 (24.4)
Cesarean section	31 (75.6)
Resuscitation – n (%)	
Yes	13 (31.7)
Nutritional status at birth– n (%)	
SGA	10 (24.4)
AGA	31 (75.6)
Neonatal infection – n (%)	
	21 (51.2)
Respiratory morbidity – n (%)	
	18 (43.9)
Apnea – n (%)	
	24 (58.5)

P25–P75, 25th–75th percentile; SD, standard deviation, SGA, small for gestational age; AGA, appropriate for gestational age.

Results

Neonatal characteristics of the participants are shown in Table 1.

Regarding sleep characteristics of preterm infants at 6 and 12 months of corrected age, differences were found in sleep position, with a significantly higher number of infants sleeping on their bellies at 12 months of age compared with 6 months. Also, there was a decrease in daytime sleep duration concomitant with a consolidation of nocturnal sleep (fewer nighttime awakenings and shorter awake periods) (Table 2).

As for motor development, both the AIMS and Denver II showed that most infants had suspected delay/atypical development at 6 and 12 months of corrected age, with no difference between the scales (p = 1.000). There was good agreement between the two scales at 6 months (κ = 0.71) and at 12 months (κ = 0.73) of corrected age (Supplementary material, Table 1).

At 6 months of corrected age, there was an association between atypical development (Denver II)/suspected

Table 2 Sleep characteristics of preterm infants at 6 and 12 months of corrected age.

Sleep characteristics (BISQ scale)[a]	6 months (n = 40)	12 months (n = 40)	p
Birth order – n (%)			0.655[b]
Oldest	13 (32.5)	12 (30.0)	
Middle	0 (0.0)	1 (2.5)	
Youngest	27 (67.5)	27 (67.5)	
Sleeping arrangement – n (%)			0.736[b]
Infant crib in a separate room	10 (25.0)	11 (27.5)	
Infant crib in parents' room	1 (2.5)	2 (5.0)	
In parents' bed	17 (42.5)	16 (40.0)	
Infant crib in room with sibling	10 (25.0)	9 (22.5)	
Other	2 (5.0)	2 (5.0)	
Sleep position[c] – n (%)			
On the child's belly	4 (10.0)	13 (32.5)	**0.012**[b]
On the child's side	13 (32.5)	20 (50.0)	0.167[b]
On the child's back	25 (62.5)	19 (47.5)	0.180[b]
Nocturnal sleep duration (h) – mean ± SD	9.2 ± 1.2	9.1 ± 1.7	0.832[d]
Daytime sleep duration (min) – mean ± SD	151 ± 65.2	121 ± 50.6	**0.021**[d]
No. of nighttime awakenings – median (P25–P75)	2 (1–3)	1 (0–2)	**0.003**[e]
Duration of nocturnal wakefulness (min) – median (P25–P75)	20 (0–40)	5 (0–30)	**0.043**[e]
Settling time until falling asleep (min) – median (P25–P75)	30 (16–56)	30 (16–30)	0.474[e]
Method of falling asleep – n (%)			0.064[b]
While feeding	18 (45.0)	14 (35.0)	
Being rocked	11 (27.5)	10 (25.0)	
Being held	1 (2.5)	1 (2.5)	
In bed alone	5 (12.5)	12 (30.0)	
In bed near parents	5 (12.5)	3 (7.5)	
Nocturnal sleep-onset time – median (P25–P75)	21.5 (21–22.5)	21.5 (21–22.5)	0.694[e]
The child's sleep is considered – n (%)			0.881[b]
A very serious problem	3 (7.5)	3 (7.5)	
A small problem	7 (17.5)	5 (12.5)	
Not a problem at all	30 (75.0)	32 (80.0)	

Bold indicates statistical significance.
BISQ, Brief Infant Sleep Questionnaire; P25–P75, 25th–75th percentile; SD, standard deviation.
[a] One family refused to answer the BISQ.
[b] Calculated by McNemar test.
[c] Multiple answers allowed.
[d] Calculated by Student's *t* test for paired samples.
[e] Calculated by Wilcoxon test.

delay (AIMS) and lateral sleep position, higher number of nighttime awakenings, and longer awake periods. Suspected delay (AIMS) was also significantly associated with having the child's sleep considered a problem by the parents (Table 3). At 12 months of corrected age, no significant association was found between sleep characteristics and motor development (Supplementary material, Table 2).

At 4–5 years of chronological age, of the original study group of 41 preterm infants, five families dropped out of the study, resulting in a sample of 36 children for analysis at age 4–5 years. The sociodemographic characteristics and data on the sleep characteristics and motor development of the participants at this stage of the study are provided as Supplementary material (Tables 3 and 4). Based on an SDSC score >39 as the cutoff point for the presence of sleep disorders, 18 (50.0%) of the 36 preterm infants had some sleep disturbance. Regarding motor development, as assessed by the PEDI, the suspected delay observed at 6 and 12 months of corrected age was reversed.

The correlation between sleep quality and motor development at 4–5 years of chronological age is shown in Table 4. Higher PEDI scores in self-care were associated with higher SDSC scores in disorders of arousal and sleep hyperhidrosis.

Discussion

We hypothesized that sleep disturbances of low-birth-weight infants born preterm would correlate with delayed motor development at 6 and 12 months of corrected age, affecting later development at 4–5 years of chronological age. Our hypothesis was not confirmed. The results showed that sleep disturbances observed at 6 months, including greater number of nighttime awakenings and longer awake periods, improved as infants grew older. Also, the suspected delay/atypical motor development at 6 and 12 months was no longer observed at 4–5 years of age.

Only a few studies assessing overall motor development and sleep characteristics in healthy preterm infants have

Table 3 Association between motor development (Denver II and AIMS) and sleep quality at 6 months of corrected age in preterm infants.

Sleep quality (BISQ scale)[a]	Denver II			AIMS		
	Normal (n = 11)	Atypical development (n = 29)	p	Normal (n = 14)	Suspected delay (n = 26)	p
Birth order – n (%)			0.068[b]			0.316[b]
Oldest	1 (9.1)	12 (41.4)		3 (21.4)	10 (38.5)	
Youngest	10 (90.9)	17 (58.6)		11 (78.6)	16 (61.5)	
Sleeping arrangement – n (%)			0.720[c]			0.714[c]
Infant crib in a separate room	4 (36.4)	6 (20.7)		4 (28.6)	6 (23.1)	
Infant crib in parents' room	0 (0.0)	1 (3.4)		0 (0.0)	1 (3.8)	
In parents' bed	4 (36.4)	13 (44.8)		7 (50.0)	10 (38.5)	
Infant crib in room with sibling	3 (27.3)	7 (24.1)		3 (21.4)	7 (26.9)	
Other	0 (0.0)	2 (6.9)		0 (0.0)	2 (7.7)	
Sleep position[d] – n (%)						
On the child's belly	1 (9.1)	3 (10.3)	1.000[b]	1 (7.1)	3 (11.5)	1.000[b]
On the child's side	7 (63.6)	6 (20.7)	**0.020**[b]	9 (64.3)	4 (15.4)	**0.004**[b]
On the child's back	4 (36.4)	21 (72.4)	0.065[b]	5 (35.7)	20 (76.9)	**0.026**[b]
Nocturnal sleep duration (h) – mean ± SD	8.8 ± 0.8	9.3 ± 1.3	0.263[e]	8.8 ± 1.1	9.4 ± 1.3	0.109[e]
Daytime sleep duration (min) – mean ± SD	138 ± 45.9	156 ± 71.3	0.440[e]	150 ± 85.1	151.3 ± 53.7	0.951[e]
No. of nighttime awakenings – median (P25–P75)	1 (0–2)	2 (1–3)	**0.006**[f]	1 (0–2)	2 (1–3)	**0.008**[f]
Duration of nocturnal wakefulness (min) – median (P25–P75)	0 (0–20)	30 (3–53)	**0.015**[f]	0 (0–23)	30 (4–60)	**0.014**[f]
Settling time until falling asleep (min) – median (P25–P75)	30 (20–60)	30 (13–53)	0.788[f]	30 (18–45)	30 (14–60)	0.747[f]
Method of falling asleep – n (%)			0.611[c]			0.277[c]
While feeding	4 (36.4)	14 (48.3)		5 (35.7)	13 (50.0)	
Being rocked	5 (45.5)	6 (20.7)		6 (42.9)	5 (19.2)	
Being held	0 (0.0)	1 (3.4)		1 (7.1)	0 (0.0)	
In bed alone	1 (9.1)	4 (13.8)		1 (7.1)	4 (15.4)	
In bed near parents	1 (9.1)	4 (13.8)		1 (7.1)	4 (15.4)	
Nocturnal sleep-onset time – median (P25–P75)	22 (21–23)	21.5 (21–22)	0.352[f]	21 (21–23)	21.5 (21–23)	0.624[f]
The child's sleep is considered – n (%)			0.080[c]			**0.028**[c]
A very serious problem	0 (0.0)	3 (10.3)		0 (0.0)	3 (11.5)	
A small problem	0 (0.0)	7 (24.1)		0 (0.0)	7 (26.9)	
Not a problem at all	11 (100)	19 (65.5)		14 (100)	16 (61.5)	

Bold indicates statistical significance.

AIMS, Alberta Infant Motor Scale; BISQ, Brief Infant Sleep Questionnaire; Denver II, Denver Developmental Screening Test II; P25–P75, 25th–75th percentile; SD, standard deviation.

[a] One family refused to answer the BISQ.

[b] Calculated by Fisher's exact test.

[c] Calculated by Pearson's chi-square test.

[d] Multiple answers allowed.

[e] Calculated by Student's *t* test for independent samples.

[f] Calculated by Mann–Whitney test.

Table 4 Correlations between sleep quality and motor development at 4-5 years of chronological age in preterm infants.

Sleep quality(SDSC factor)		Motor development (PEDI score)		
		Self-care	Mobility	Social function
Disorders of initiating and maintaining sleep	r	−0.115	0.079	−0.230
	p	0.532	0.669	0.205
Sleep breathing disorders	r	−0.034	0.021	−0.271
	p	0.854	0.911	0.133
Disorders of arousal	r	**0.363**	0.071	0.145
	p	**0.041**	0.698	0.428
Sleep-wake transition disorders	r	0.100	0.061	−0.156
	p	0.585	0.740	0.394
Disorders of excessive somnolence	r	−0.278	−0.042	−0.332
	p	0.123	0.820	0.063
Sleep hyperhidrosis	r	**0.383**	0.144	0.226
	p	**0.031**	0.431	0.214
Overall score	r	0.121	0.102	−0.172
	p	0.508	0.577	0.348

Bold indicates statistical significance.
PEDI, Pediatric Evaluation of Disability Inventory; r, Pearson's correlation coefficient; SDSC, Sleep Disturbance Scale for Children.

been conducted, suggesting an impact of sleep quality on developmental outcomes. A retrospective longitudinal study of 111 preterm infants (<34 weeks gestational age) with low birth weight (<1500 g) found that sleep state development in the preterm period, assessed weekly by observing 2 -h inter-feeding periods from NICU admission to discharge, was associated with weight and body mass index growth trajectories across early childhood (1–27 months of corrected age).[23] In a study comparing preterm vs full-term children at 2 years of age, preterm children had more sleep problems during the night, such as restlessness and breathing problems, and these problems were correlated with increased motor activity, decreased social orientation and attention, and increased negative emotionality.[11] In contrast, in the present study, the suspected delay/atypical development observed at 6 and 12 months of age did not appear to affect later development of motor skills at 4–5 years of chronological age. However, PEDI self-care correlated directly with SDSC disorders of arousal. Disorders of arousal in the first year of life are believed to be comorbid with some developmental illnesses, with strong suspicion that failure to arouse to an hypoxic stimulus is instrumental in sudden infant death syndrome.[24] Contextual factors such as ambient temperature or even severe systemic diseases may reduce or compound risk, but such factors were not assessed in our study. Further investigation is required to explain this finding, preferably using a larger sample.

Also noteworthy is the finding that, at 6 months of corrected age, suspected delay (AIMS) was associated with having the child's sleep considered a problem by the parents. A Swedish study investigating how parents perceived their preterm infants' sleep, and their own, during NICU stay and after discharge found an association between mothers' sleeping problems during their infants' hospitalization and later perceptions of sleep problems in their children.[25] The authors suggest that parents need support in the NICU to optimize their own sleep in an attempt to prevent them from perceiving their child's sleeping patterns as a problem later.

Interestingly, for both motor development scale and screening test used in the present study, lateral sleep position was associated with atypical development at 6 months of corrected age. Since most studied infants slept on their backs, this position may have had an indirect influence on the pattern of motor development compared with other sleep positions. In children with birth weight <1750 g, the supine position during sleep was associated with greater difficulty maintaining the head elevated at 56 weeks of age.[26] Conversely, the prone position is a well-known risk factor for sudden infant death syndrome, and compensatory strategies are needed to prevent delayed acquisition of head control.[26] In Brazil, it was not until 2009 that a nationwide campaign was launched to educate pediatricians about safe infant sleep practices. According to data from a survey conducted in 2013, most pediatricians (67.5%) recommended lateral sleep position before the 2009 campaign, falling to 10.4% after the campaign. However, concerning current advice provided to parents, pediatricians aged >60 years and those with more than 10 years of professional practice more frequently recommended lateral sleep position.[27] Therefore, we can assume that infants were sleeping on their side because parents were following the pediatrician's advice, a practice that only now is beginning to change consistently.

This study has several limitations. A major drawback of longitudinal studies is that sample size tends to be smaller than in cross-sectional studies, which do not require patient follow-up. Although much effort was put into recruitment and follow-up to minimize dropout, 5 families dropped out of the original study group of 41 preterm infants, which resulted in a small sample size for analysis at age 4–5 years, as is the case in virtually all studies of this type. Despite having appropriate statistical power based on the pilot study, the small sample size did not allow detailed subgroup analyses. Also, although polysomnography is the gold standard to diagnose sleep disorders, its use in Brazil is limited by the high cost and small number of specialized centers that can perform this test, especially in infants.[22] Actigraphy is a non-invasive method that has been used to assess sleep patterns in pediatric patients. However, this tool has shown low specificity in detecting wake after sleep onset and limited validity for estimating sleep onset latency and daytime napping.[28] The BISQ and SDSC are among the questionnaires that present proper psychometric parameters to measure sleep quality and have been validated for use in Brazil. The fact that these instruments rely on parental report may be considered a limitation, but there is evidence of a good correlation between parental report of infant sleep behavior and objective measures, such as actigraphy.[29,30] As for the assessment of motor development, although the Bayley Scales of Infant Development are the gold standard for this purpose, a version of these instruments had not been validated for use in the Brazilian pediatric population at the time the study was conducted. Also, the use of different scales to assess both sleep and motor development at different time points (6 and 12 months vs. 4–5 years of age) may have led to failures in the longitudinal description of the evaluated characteristics. However, these scales are appropriate for the ages assessed here. Finally, we did not assess mother-child interaction, which is known to have an impact on the child's behavior and development outcomes.

In conclusion, sleep quality correlated with delayed/atypical motor development only at 6 months of corrected age in preterm infants with low birth weight. Sleep quality at 6 months of corrected age requires special attention in preterm infants, especially in the presence of nighttime awakenings. Delayed motor development in preterm infants was more evident during the first 12 months of corrected age, but this did not appear to affect motor development later in life, at 4–5 years of age.

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Conflicts of interest

The authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jped.2019.10.010.

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