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Assessment of pain and sleep symptoms in children at high risk for cerebral palsy in a pediatric neurodevelopmental clinic: Implications for future quality improvement interventions

Lisa Letzkus, PhD, RN, CPNP, AC [a,*], Katheryn Frazier, MD [a], Jessica Keim-Malpass, PhD, RN [b]

[a] University of Virginia School of Medicine, Department of Pediatrics, Neurodevelopmental and Behavioral Pediatrics, UVA Children's, Charlottesville, VA, USA
[b] University of Virginia School of Nursing, Charlottesville, VA, USA

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ABSTRACT

Children with cerebral palsy (CP) often experience distressing symptoms. It is estimated that 3 in 4 have chronic pain and 1 in 5 have a sleep disorder, with the highest frequency and severity occurring in children with the greatest impairment. Sleep impairment and pain can adversely impact activities, participation and quality of life; however, prevalence of these symptoms in children at risk for CP < 2 years of age remain unknown. The objective of this project was to develop a baseline understanding of the presence of sleep and pain symptoms among children <2 years at high risk for CP to establish a baseline estimate for future quality improvement initiatives. A retrospective chart review was performed on a convenience sample of 50 children <2 years of age that were determined to be high risk for CP. This was determined through a standardized Hammersmith Infant Neurological Evaluation (HINE) global score of less than 56 performed as part of routine care. Descriptive statistics were used to explore the sample. A nonparametric test was used to evaluate the differences between groups. Pain and sleep problems were frequently reported in our sample (38% sleep problems and 32% pain). There were also significant differences between reported symptoms and the HINE. Reported symptoms were associated with lower HINE scores. Sleep and pain are frequent symptoms in children at risk for cerebral palsy. Early identification of these symptoms can lead to clinic-level intervention which may include pharmacological and non-pharmacological management strategies that improve outcomes for children at high risk for CP.
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Introduction

Cerebral palsy (CP) is the most common physical disability in childhood and can be defined as "a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain" (Rosenbaum et al., 2007). Comorbidities and unpleasant symptoms are common in this population and can impact function (Novak et al., 2017; Novak et al., 2020). Sleep disturbances and pain are frequently reported symptoms in children with CP. It is estimated that 3 in 4 have chronic pain and 1 in 5 have a sleep disorder, with the highest frequency and severity occurring in children with the greatest impairment (Novak et al., 2020). Consequences of unrecognized and untreated symptoms can be detrimental. Pain can negatively influence the child's quality of life and participation in activities such as therapies, school, and play/leisure,; while sleep problems can have lasting behavioral and cognitive sequela (Novak et al., 2012; Shay et al., 2014). Sleep problems also affect the parents' health and is associated with poor quality of parental sleep and increased risk for maternal depression (Sandella et al., 2011; Wayte et al., 2012).

Historically, the diagnosis of CP was made between 12 and 24 months of age which delayed intervention, but now the diagnosis can be made before 6 months of age by applying early detection of CP guidelines (Novak et al., 2017). To make an early clinical diagnosis before 6 months of age, a combination of clinical reasoning, central nervous system imaging, and standardized neurological and motor assessments are used. Early identification is important as there are now CP-specific early interventions that can improve motor, cognition, and communication skills, as well as interventions to prevent secondary impairments and minimize complications (Novak et al., 2017).

Two systematic reviews were recently conducted using the rigorous GRADE methodology to update the science for assessment and intervention for sleep and pain problems in children less than two years of age with or at high risk for CP (Alonso-Coello, Oxman, et al., 2016; Alonso-Coello, Schünemann, et al., 2016; Letzkus et al., 2021; Tanner et al., 2021). The findings highlight the gaps and standardization needed

* Corresponding author at: Neurodevelopmental and Behavioral Pediatrics, UVA Children's, PO BOX 800828, Charlottesville, VA 22908, USA.
E-mail address: lmc8c@virginia.edu (L. Letzkus).

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to address these two symptoms in this population. A conditional GRADE recommendation was made in favor of parental-report for pain assessment (Letzkus et al., 2021). Polysomnography was identified as the gold standard for sleep assessment and a conditional recommendation was made that clinical assessment of sleep includes both intrinsic and extrinsic factors (Tanner et al., 2021). No pharmacological agents were identified that safely and effectively improve sleep and pain in this population. These systematic reviews also integrated findings with an online survey that was distributed to parents of children with CP. Caregiver comfort measures were ranked the highest for strategies for management of pain and sleep problems by parents (Letzkus et al., 2021; Tanner et al., 2021).

Best available evidence on interventions to prevent and treat children with CP, including interventions for pain and sleep, was recently published in a systematic review; no interventions for pain and sleep symptoms were in the "Do it" category but there were several interventions in the "Probably do it" category (Novak et al., 2020). It is important to note, this systematic review included all intervention for all ages of children with CP and should not be applied to the younger age group without thoughtful consideration (Novak et al., 2020).

To date, there has been a proliferation of pediatric complex care and neurodevelopmental clinics that care for children at high risk for CP (Van Cleave et al., 2016). As these clinics continue to grow, they have been tasked with providing systematic coverage for multiple chronic complex conditions as well as management of evolving symptoms and symptom clusters such as pain and sleep. Effective treatment strategies for decreasing the burden of pain and sleep symptoms in children <2 years at high-risk of CP cannot be evaluated and identified until more is known on the occurrence of symptoms in this population. Identification of adverse pain and sleep symptom presence is the first step that may lead to treatment strategies that help decrease symptom burden for children less than two years of age with CP. Thus, the purpose of this analysis was to develop a baseline understanding of the presence of sleep and pain symptoms among children less than 2 years at right risk for CP as documented in the electronic medical record (EMR) by providers during routine clinic encounters in an interdisciplinary high-risk infant developmental follow-up program. Developing an ongoing process for routine and systematic assessment of this important symptom cluster is a vital first step in being able to evaluate interventions to improve the successful assessment and integration of developmentally-appropriate interventions.

Methods

A retrospective chart review was performed on a convenience sample of 50 children <2 years of age that were determined to be high risk for CP. The children all received care at UVA Children's Early Development Clinic and had the standardized Hammersmith Infant Neurological Evaluation (HINE) performed as part of routine care (2018–2019). All children had scored ≤56 on the HINE which is indicative of high risk for CP (Maitre et al., 2016; Novak et al., 2017; Romeo et al., 2008). Chart review was performed and the presence of pain and sleep problems were extracted based on the neurodevelopmental pediatric provider's clinic documentation. Demographic characteristics included gestational age at birth and gender. The global HINE score was recorded. This project did not require institutional review board approval as the project was used for improvement of clinical care per the University of Virginia Determination of Human Subject Research.

The UVA Children's Early Development Clinic is a coordinated and comprehensive interdisciplinary follow up program for infants at risk for developmental challenges. The goals of the program are to monitor developmental progress over time, perform standardized neurodevelopmental assessments, and ensure children are receiving appropriate and timely intervention with the goal of promoting optimal development and quality of life. Interdisciplinary team members include: developmental pediatricians and nurse practitioners, physical, occupational, speech and language therapists, pediatric psychologist, dietician and a designated nurse coordinator. Social work is also available.

Criteria for referral is based on risk factors, which then determine whether early or routine follow up is indicated (Table 1). The program follows children up to 2 years of age (24 months corrected), at which time need for ongoing follow-up in general neurodevelopmental clinic or a subspecialty clinic (i.e. Cerebral Palsy clinic) is reviewed by the team and discussed with the family. Clinic visits and relevant developmental assessments are performed at the following intervals (Fig. 1 algorithm) adapted from the Early Detection of CP guidelines.

The HINE is a quantitative standardized neurological evaluation that is a recommended tool for early detection of CP (Maitre et al., 2016; Novak et al., 2017; Romeo et al., 2008). Twenty-six items assess cranial function, posture, quality and quantity of movements, muscle tone, reflexes and reactions. Each item is scored individually 0–3 with a sum score of all items ranging from 0 to 78. The lower the global score, the poorer the motor function. A global score ≤ 56 indicates a child is at high risk for CP; with risk further categorized into risk of moderate motor impairment (41–60) or risk of severe motor impairment (≤40) (Romeo et al., 2009). The HINE allows for identification of early signs of CP and has demonstrated a predictive value of 96% (Novak et al., 2017). Assessment can be performed on children ages 2–24 months corrected gestational age. The test requires specialized training and takes about 10 min to administer in the clinic setting. Developmental pediatricians and nurse practitioners at UVA administer this assessment as part of routine clinical care to monitor motor trajectory of infants deemed at risk based on birth and medical history factors.

Statistical analysis was performed using SPSS v27. Pain and sleep problems were coded as yes/no. Descriptive statistics were used to explore the sample. A nonparametric (Mann Whitney U) test was used to evaluate the differences between groups.

Results

Fifty children <2 years of age with a HINE global score ≤ 56 were included for analysis. The mean gestation age at birth was 31.90 ± 5.93 weeks; 66% ($n = 33$) were male. The mean global HINE score

Table 1
Follow up criteria to Early Development Program.

Early Follow up occurs at 3 months CGA (any of the following)	Routine follow occurs at 6 months CGA (any of the following):
• <30 weeks' gestation • <1000 g birthweight • Hypoxic ischemic encephalopathy ± cooling • Bronchopulmonary dysplasia still requiring mechanical ventilation at 36 weeks CGA • Major brain lesions (periventricular leukomalacia, parenchymal lesions, grade 3 or 4 IVH, infarct) • Congenital brain malformations • Cramped synchronized, poor repertoire per general movement assessment or abnormal neurologic exam • Necrotizing enterocolitis requiring surgery • Extracorporeal membrane oxygenation • All Neuro-NICU patients unless specified otherwise • Other (i.e. maternal substance use disorder, foster care, maternal mental health concerns, provider or therapist concern	• >30 to <35 weeks' gestation • ≥1000 to <1500 g birthweight • Minor brain lesions (i.e. benign enlargement of sub-arachnoid spaces, IVH grade 1 or 2 with no post-hemorrhagic ventricular dilatation

Legend: Corrected gestational age (CGA); intraventricular hemorrhage (IVH); Neonatal intensive care unit (NICU).

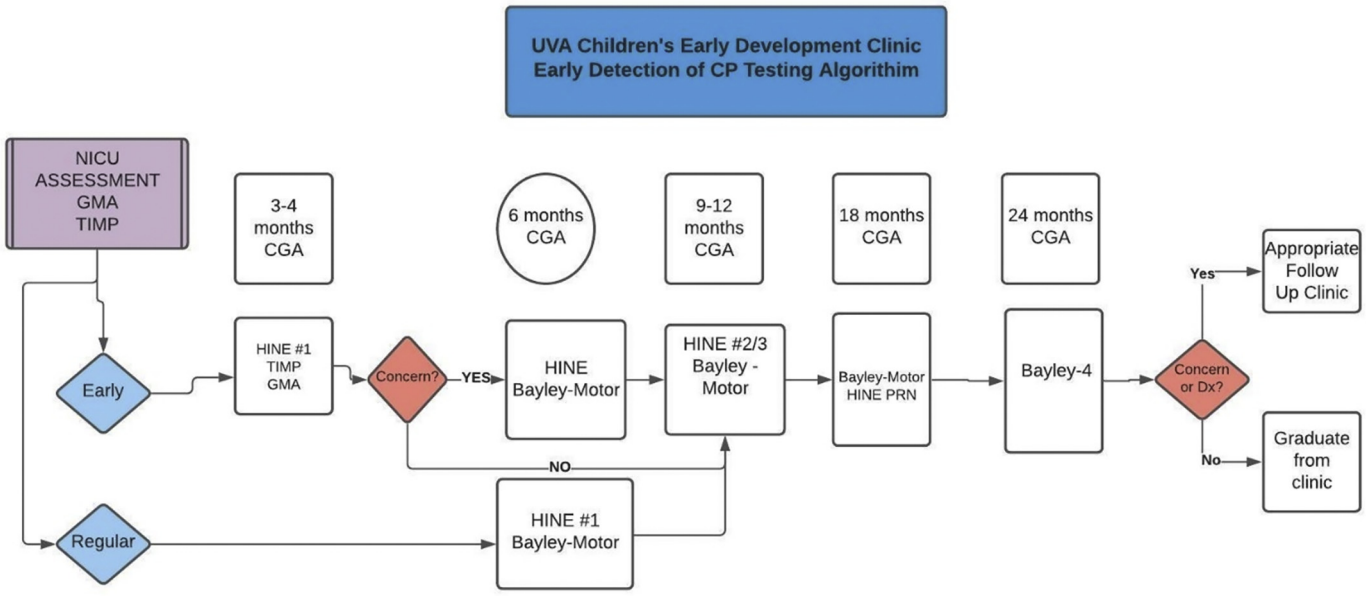

Fig. 1. UVa Children's Early Development Clinic early detection of cerebral palsy (CP) developmental testing algorithm.
Legend: Bayley Scales of Infant and Toddler Development 4th edition motor component (Bayley motor) Corrected Gestational Age (CGA); Diagnosis (Dx); General Movement Assessment (GMA); Hammersmith Infant Neurological Evaluation (HINE); Neonatal intensive care unit (NICU); Test of Infant Motor Performance (TIMP).

was 45.72 ± 9.21. Thirty-eight percent ($n = 19$) had reported sleep problems and 32% ($n = 16$) had reported pain problems. Forty six percent reported at least one symptom of pain or sleep problems while 24% reported both symptoms. Global HINE scores based on symptom presence are featured in Table 2. There was a significant difference noted between sleep and global HINE scores ($p = 0.005$) and a significant difference between pain and global HINE scores ($p = 0.001$; Fig. 2). There was also a significant difference between global HINE scores and having both symptoms ($p = 0.003$) and having either sleep problems or pain, ($p = 0.009$; Fig. 2). There were no significant difference between sleep and gestational age ($p = 0.288$) or between pain and gestational age ($p = 0.876$). There was also not a significant difference between both symptoms and gestational age ($p = 0.820$); or either symptom and gestational age ($p = 0.324$)

Discussion

This baseline symptom assessment detected a high prevalence of pain (32%) and sleep problems (39%) documented in our convenience sample of 50 children <2 years of age and at risk for CP (HINE score ≤ 56). In addition, 24% of the sample reported both pain and sleep problems. Our findings are congruent with literature published in older children with CP, who frequently report unpleasant pain and sleep symptoms (Novak et al., 2020). In older children with CP, these symptoms are associated with decreased functional outcomes and decreased quality of life (Novak et al., 2012; Novak et al., 2020).

Our findings noted a difference in symptom presence and HINE score (Table 2, Fig. 2). Those with sleep problems and pain had lower HINE scores compared to those that did not report these symptoms. Children in the sample that reported both pain and sleep symptoms had the lowest HINE scores (38 ± 10.189) and were at the greatest risk for severe motor impairment (HINE score < 40) (Romeo et al., 2009). This preliminary finding is also supported by the literature that the highest frequency and severity of symptoms occur in children with the greatest motor impairment (Novak et al., 2012; Novak et al., 2020).

Table 2
Differences between symptom presence and Hammersmith Infant Neurological Evaluation (HINE) global scores.

Symptom Presence	$N = 50$	Global HINE Score	p-value
Sleep			0.005*
Yes	19	41.05 ± 9.606	
No	31	48.58 ± 7.809	
Pain			0.001*
Yes	16	40.44 ± 10.217	
No	34	48.21 ± 7.659	
Sleep or Pain (either)			0.009*
Yes	23	42.22 ± 9.410	
No	27	48.70 ± 8.057	
Both			0.003*
Yes	12	38 ± 10.189	
No	38	48.16 ± 7.489	

* p-value <0.05.

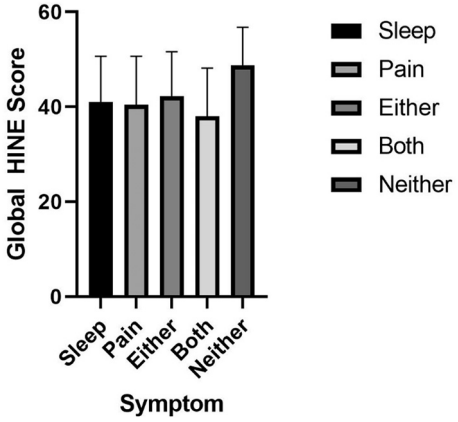

Fig. 2. Differences between reported symptom presence and global Hammersmith Infant Neurological Evaluation (HINE) scores. Means and standard deviations displayed.

Implications to practice

Pain and sleep symptoms are common in children <2 years of age at high risk for CP. Team members caring for these children should be

aware and screen for these symptoms as they can adversely impact activity, participation and quality of life (Novak et al., 2012; Shay et al., 2014; (Sandella et al., 2011; Wayte et al., 2012). Parental report is a first step in assessing for the presence of these symptoms (Letzkus et al., 2021; Tanner et al., 2021). There will be times when pharmacological intervention is needed in severe cases and a thoughtful conversation with parents and other team members to discuss the risks and potential benefits should be encouraged. When interventions are initiative, it is important to determine how to monitor the effect of interventions which can include incorporating standardizes questionnaires or screenings, obtaining a detailed history and performing a thorough physical examination at each follow up visit.

Limitations

Limitations of this single site project include the sampling method and small sample size. A convenience sample was used of children that had a HINE performed at follow up when they were < 2 years of age. A more comprehensive retrospective review of demographic and clinical data will be helpful in future research studies; however, that was out of the scope for this focused baseline assessment to develop future quality improvement interventions. It will also be useful to try to track and categorize these symptoms over time as well as take into consideration variations in developmental trajectories between patients. Furthermore, the impact of these symptoms on severity of CP remains unclear. Evidence based strategies and successful self-management techniques to intervene and decrease symptom burden is limited in children at risk for CP.

Conclusion

The UVA Children's Early Development Program is using this baseline data to develop and implement strategies to further monitor and address pain and sleep symptoms in children <2 years of age at high risk for CP. Based on the results of this baseline assessment, attention has been made leveraging the history and physical examination findings in addition to documentation of the presence of assessing for these symptoms consistently in the ambulatory setting. We are also incorporating a standardized pain assessment which will be performed by nursing and providers as well as obtaining parent report. Early identification of these symptoms can lead to intervention which may include pharmacological and non-pharmacological management strategies that improve outcomes for children at high risk for CP. There is immense opportunity to integrate standardized routine assessment practices involving patient-reported outcomes into EMRs (Girgis et al., 2017). Further work is needed to automatically integrate time series and symptom cluster trends within the electronic medical record to assist clinicians in assessing for clinically-meaningful transitions in symptoms or unmet symptom needs. Finally, pairing relevant symptom phenotypes with early intervention for optimal neurodevelopmental outcomes is needed.

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