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ORIGINAL ARTICLE

Clinical reliability and validity of the N-PASS: neonatal pain, agitation and sedation scale with prolonged pain

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Objective: To establish beginning evidence of clinical validity and reliability of the Neonatal Pain, Agitation and Sedation Scale (N-PASS) in neonates with prolonged pain postoperatively and during mechanical ventilation.

Study Design: Prospective psychometric evaluation. Two nurses administered the N-PASS simultaneously and independently before and after pharmacologic interventions for pain or sedation. One nurse also administered the premature infant pain profile (PIPP) concurrently with the N-PASS. The setting consisted of 50-bed level III neonatal intensive care unit. Convenience sample of 72 observations of 46 ventilated and/or postoperative infants, 0 to 100 days of age, gestational age 23 to 40 weeks was used. Outcome measures comprised convergent and construct validity, interrater reliability and internal consistency.

Result: Interrater reliability measured by intraclass coefficients of 0.85 to 0.95 was high ($P<0.001$ to 0.0001). Convergent validity was demonstrated by correlation with the PIPP scores (Spearman's rank correlation coefficient of 0.83 at high pain scores, 0.61 at low pain scores). Internal consistency, measured by Cronbach's α, was evident with pain scores (0.82), and with sedation scores (0.87). Construct validity was established via the Wilcoxon signed-rank test, comparing the distribution of N-PASS scores before and after pharmacologic intervention showing pain scores of 4.86 (3.38) and 1.81 (1.53) (mean (s.d.), $P<0.0001$) and sedation scores of 0.85 (1.66) and −2.78 (2.81) ($P<0.0001$) for pre- and postintervention assessments, respectively.

Conclusions: This research provides beginning evidence that the N-PASS is a valid and reliable tool for assessing pain/agitation and sedation in ventilated and/or postoperative infants 0 to 100 days of age, and 23 weeks gestation and above.

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Introduction

Pain and sedation assessment in the neonatal intensive care unit (NICU) is an essential and often difficult process. Infants, incapable of verbal self-report, provide behavioral and physiological cues to indicate the presence of pain and sedation. Infants in the NICU experience multiple acute/procedural pain events as well as prolonged pain and distress postoperatively and due to mechanical ventilation. Analgesics and sedatives are commonly administered to infants in the NICU with wide variance in practice among units. Assessment of the infant's level of pain and sedation assists in clinical management and evaluation of therapies. Clinical goals include analgesics to relieve pain, and may include analgesics and/or sedatives to attain sedation. Optimal levels of sedation are not known for preterm or full-term infants in various situations in the NICU.[1] The American Academy of Pediatrics and Canadian Paediatric Society policy statement on the prevention and management of pain in the neonate recommends routine pain assessment in neonates, and summarizes nine commonly used pain assessment scales, including the Neonatal Pain, Agitation and Sedation Scale (N-PASS).[2] Sedation is a concept less studied in the neonatal population; no sedation assessment tool was available for infants. Cochrane's review of sedative use in neonates recognizes the need for a validated neonatal sedation tool.[3]

Pain in the NICU can be categorized into three types: (1) acute-procedural pain, where pain results from a specific nociceptive event that is self-limited, (2) acute-prolonged pain, where there is a clear stimulus, with a clearly definable beginning and an expected end point and (3) chronic pain, a pathological pain state without apparent biological value that has persisted beyond the normal tissue healing time, usually 3 months.[4] These three types of pain are not well delineated, and may occur simultaneously. Several infant pain assessment tools have been developed for acute-procedural pain; few are designed for prolonged or chronic pain.

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Although neonates are routinely sedated in the NICU, a sedation assessment tool had not been developed for clinical or research use. Sedation is defined as a calm tranquil state that allays anxiety and excitement.[5] The American Society of Anesthesiologists delineates a continuum of sedation from minimal (anxiolysis) to general anesthesia.[6] In this continuum, levels of sedation are evaluated by assessing responsiveness, airway, spontaneous ventilation and cardiovascular function, items particularly important in the perioperative or procedural/diagnostic situations. Optimal sedation levels are not known for neonates, with wide variations in practice. Postoperative infants require analgesia; some are sedated as a side effect of analgesia or the goal may be sedation in addition to analgesia. Goals for ventilated infants include analgesia and possibly sedation. The N-PASS was developed as a clinically relevant tool to assess primarily acute-prolonged pain and also sedation in infants, with further research planned to evaluate the N-PASS with acute-procedural and chronic pain states. This study was designed to investigate the validity and reliability of the N-PASS tool with acute-prolonged pain and sedation; specifically, mechanical ventilation and/or postoperative states.

Methods

Tool development

The literature was searched for clinically usable pain and sedation assessment tools, suited to all NICU infants, and applicable in all pain states. Many tools, such as the Premature Infant Pain Profile (PIPP)[7] or Neonatal Infant Pain Scale[8] are excellent tools for acute pain but are more difficult to apply to prolonged pain. The Crying, Requires oxygen for saturation, Increased vital signs, Expression, Sleepless (CRIES) tool, developed for postoperative pain, does not appear to be valid for the premature infant.[9] The Echelle Douleur Inconfort Nouveau-Ne (EDIN) tool, more recently developed to assess prolonged pain in the ventilated premature infant, does not assess sedation levels.[10] Detailed reviews of pain assessment tools are available elsewhere.[4,11]

The N-PASS was designed as a clinically useful tool for all infants in the NICU. Indicators were chosen from literature review and expert opinion based on clinical applicability, ease of assessment and established validity. Consistent with the hospital standard, a 0 to 10 scale was selected. Five criteria are graded 0, 1 or 2 for pain/agitation and 0, −1 or −2 for sedation. A high pain/agitation score indicates more frequent or intense behaviors, and a low sedation score indicates a decreased response to stimulation, or a deeper level of sedation. Electronic cardiac and pulse oximetry monitoring are helpful, but not required, as auscultated heart rate and/or respiratory rate facilitate use with well infants in the NICU or the newborn nursery.

The pain assessment portion of the N-PASS is labeled 'pain/agitation' due to clinical difficulties in differentiating these two entities clinically, particularly in prolonged or chronic pain situations. Although researchers have attempted to categorize behaviors into typical of 'pain' and typical of 'agitation,' many commonalities exist. An infant who appears to be in pain or agitated should be evaluated within the context of the situation in an attempt to determine causality for the behavior, guiding treatment.

Because premature infants have a limited ability to display and maintain behavioral or physiological manifestations of pain, points are added to the preterm infant's pain score to approximate the normal response of a full-term infant.[12] Gestational age categories and points assigned are based on the PIPP tool categories.[7] Corrected gestational age determines the number of points added to the score. The sedation score does not require this adjustment as gestational age is not known to affect the premature infant's ability to exhibit signs of sedation.

Five indicators are included in the N-PASS, chosen for their established validity, clinical applicability and ease of assessment: crying/irritability, behavior/state, facial expression, extremities/tone and vital signs (heart rate, respiratory rate, blood pressure and/or oxygen saturation). Within each category, examples of criteria are provided to assist in the assignment of a numerical value. The N-PASS can be viewed at www.n-pass.com.

Behavioral and physiological manifestations of pain in the neonates have been well researched. The five indicators utilized in the N-PASS are included in various neonatal pain assessment scales.[13] Sedation indicators are less well researched. Sedated infants were observed to establish behaviors indicating sedation utilizing the same five indicators. The sedation indicators are consistent with the State Behavioral Scale, the COMFORT scale and the Modified Glasgow Coma Scale.[5,14,15] The Modified Glasgow Coma Scale evaluates level of consciousness, scoring the best eye, verbal and motor responses, and is not widely used clinically for sedation assessment. The State Behavioral Scale was tested in mechanically ventilated infants and children from 6 weeks to 6 years old, providing systematic description of the sedation–agitation continuum in young pediatric patients supported on mechanical ventilation. Indicators of sedation and agitation included in this scale are respiratory drive, response to ventilation, coughing, best response to stimulation, attentiveness to care provider, tolerance to care, consolability and movement after being consoled.[5] The COMFORT tool was developed to assess distress in the Pediatric Intensive Care Unit and has been researched in the 0- to 3-year-old postoperative population.[14] The COMFORT indicators include alertness, calmness, respiratory response, movement, mean arterial blood pressure, heart rate, muscle tone and facial expression. Low scores indicate coma or sedation, moderate scores indicate lack of distress and high scores indicate distress.

Crying is a distress signal, a response to both acute and prolonged pain.[16,17] A 'pain cry' is described as more persistent and higher pitched in acute pain situations, and longer in duration with prolonged pain. A decreased or absent cry is observed in a

sedated state, as the baby is less responsive.[5] Consolability is utilized in pain and sedation assessment, as an indicator of pain, pain relief and agitation.[13] Consolability is also included in the EDIN tool and the State Behavioral Scale.[5,10]

Behavior/state is assessed by observing body movements, such as arching and kicking, and the ability to rest and sleep, indicative of the general comfort level.[18–20] Lack of body movement and decreased arousal to stimuli are observed in a sedated state. The State Behavioral Scale and the COMFORT Scale include parameters of arousal and body movement.[5,14]

Facial expression has been extensively researched as a valid and reliable pain behavior.[17] Facial changes indicative of pain include lowered brows drawn together, bulge between brows, eye squeeze, nasolabial furrow, nose broadened and bulging, cheeks raised and mouth open and squarish.[16,21] Due to the decreased predictability of facial expression over time, facial expressions should be combined for assessment of prolonged pain.[4] A sedated infant exhibits a decrease in facial expression with stimuli. The COMFORT tool includes a lack of facial expression as an indicator.[14]

Observing the position of the extremities, fisting/clenching, finger splay and general tone of the body assist in evaluating comfort and relaxation, and is helpful in assessing both acute and prolonged pain.[22] Flexion of the arms and legs and leg extension movements are associated with pain.[23] The sedated infant exhibits a suppression of the grasp reflex and muscle tone is decreased. The COMFORT tool includes a loss of muscle tone as an indicator.[14]

Vital sign changes are related to the autonomic stress response associated with pain.[18] Heart rate, blood pressure and respiratory rate increase above baseline in painful situations. Vital signs changes may be less useful with chronic pain, as these may return to baseline with variances among infants. Vital sign changes are the sole indicator of pain and sedation available for use during neuromuscular blockade.[13] Oxygen desaturation per pulse oximetry is observed in both acute and established pain situations.[24] For ease of assessment vital sign changes were categorized into modest increases (10 to 20% from baseline) or larger increases (>20% from baseline). A loss of variability in vital signs with stimulation and depressed ventilatory effort are physiological signs of sedation. Respiratory drive and response are sedation indicators in the State Behavioral Scale and in the COMFORT tool.[5,14] N-PASS users are instructed to choose vital sign criteria appropriate to the clinical situation.

Formatting the N-PASS utilizing the same criteria to assess both pain/agitation and sedation allows evaluation of the infant on a theoretical continuum. An infant's behavior can range from deeply sedated, to lightly sedated, to normal, to mild pain/agitation, to severe pain/agitation. Despite this theoretical continuum, pain and sedation must be evaluated and scored as separate entities since both can occur simultaneously, although it is recognized that increasing levels of sedation may mask the infant's response to pain.[25] Clinically, infants that become sedated due to analgesics are not likely to be in pain, but pain may be masked by sedative administration. Sedation behaviors and neurological depression behaviors are similar, and neurological irritability and pain behaviors are similar, highlighting the difficulties with pain and sedation assessment in an infant with an abnormal neurological status.

Study design

The N-PASS tool was introduced into a 50-bed level III NICU following education of the nursing staff. No formal method of pain or sedation assessment was in place prior to N-PASS implementation and clinical management was based upon the subjective assessment of the team.

Following Institutional Review Board (IRB) approval, a select group of 10 nurses were further trained for data collection. Parents were informed of the study via an admission letter; the IRB determined that formal consent was not required due to the noninvasive nature of this observational study. The N-PASS and the PIPP instruments were reviewed with each data collector. The PIPP was chosen for convergent validity due to established validity and applicability with premature as well as term infants, and because there was no well researched tool for prolonged pain available for use in preterm infants at the time of this research. Although primarily an acute-procedural assessment tool, the PIPP was widely used clinically with prolonged pain at the time of data collection. The nurse scored the behavioral state category of the PIPP prior to the assessment period.

Ventilated and/or postoperative infants with prolonged pain were evaluated before and after pharmacologic intervention. Pharmacologic intervention was not controlled. Infants received an opioid and/or a sedative, based upon standard unit practices. Morphine was administered by bolus in the majority of infants to achieve analgesia and/or sedation. Lorazepam was administered when the clinical goal was sedation. The N-PASS tool was independently and concurrently administered when two data collection nurses were present, for 5 to 10 min before and 1 hour after analgesic and/or sedative administration on an infant with a pain score over 3. One nurse also administered the PIPP tool concurrently with the N-PASS.

Statistical analysis

The primary analysis focused on the reliability and validity of the sum score derived from the N-PASS instrument. Two measures of instrument reliability were used: (1) intraclass correlation coefficient (ICC), as a measure of interrater reliability and; (2) Cronbach's α, as a measure of internal consistency. The ICC corresponds to a one-way random effects model, with each neonate representing a level of the random person factor. The ICC (1, 2) model produces two different ICC estimates: one for the reliability of a single rating, and one for the reliability of the mean of two ratings.[26]

Two measures of instrument validity were applied: (1) Spearman's rank correlation between the N-PASS and the PIPP as a measure of convergent validity and (2) Wilcoxon signed-rank test to compare the distribution of N-PASS scores before and after pharmacologic intervention as a measure of construct validity.

Counts and percentages were reported for categorical variables and range; median, mean and standard deviation for continuous/ordinal data. A Spearman's rank correlation coefficient was utilized to evaluate associations between continuous/ordinal variables and N-PASS score. The Kruskal–Wallis or Wilcoxon rank-sum test was applied as appropriate to compare N-PASS scores between categorically defined groups.

Sample size

The power calculations were done in PASS2000. Data from several earlier studies of pain assessment tools indicate high interrater reliability as measured by the ICC (0.6 to 0.95).[7,9] A total of 32 neonates were evaluated for pain and sedation prior to and after intervention by two raters each. A sample size of 32 neonates (and 2 raters) achieved 80% power to detect a difference of 0.22 between the null hypothesis ICC of 0.6 and the alternative hypothesis ICC of 0.82 using an F-test with a significance level of 0.05.

A total of 46 neonates were evaluated for pain and sedation at least once by multiple raters for a total of 72 evaluations. Since different raters performed the evaluations of a given neonate, the 72 observations were treated as independent. The standard deviation of the pain scale prior to intervention was 3.4. A sample size of 72 achieved 80% power to detect a difference of 1.2 between the null hypothesis mean of 0.0 (average difference between pre- and postintervention N-PASS pain score) and the alternative hypothesis mean of 1.2 with an estimated standard deviation of 3.4 and with a significance level (α) of 0.05 using a two-sided Wilcoxon signed-rank test.

Sample

A convenience sample of intubated and/or postoperative neonates admitted to the NICU, who were receiving pharmacologic interventions, opioids, sedatives or both, were included in the study when two data collectors were present. Data collection continued until 72 data sets (before and after intervention assessments) were obtained on 46 infants. Data were collected up to three times per infant, on different days. A total of 21 infants (46%) were male and 25 (54%) were female. Twelve infants were assessed postoperatively; surgeries included bowel resection, exploratory laparatomy for necrotizing enterocolitis (NEC), esophageal atresia with tracheoesophageal fistula repair and patent ductus arteriosus ligation. Ten infants were assessed within 5 days postoperatively, two infants with prolonged pain postoperatively due to NEC were assessed at 7 to 10 days postoperatively, when their pain scores were over 3. Infants ranged from 23 to 40 weeks gestation at birth and were 0 to 100 days of age at assessment. (See Table 1 for gestational age distribution).

Table 1 Gestational age distribution

Gestational age (weeks)	*Percent*
>35	30.6
32–35	22.2
28–31	27.8
<28	19.4
Total	100

Results

Interrater reliability analysis

Pain scale. For the first observation of a neonate (prior to any intervention for pain or sedation), the ICC estimates (95% confidence interval, CI) of the pain scale were 0.95 (0.90, 0.97) and 0.97 (0.95, 0.99) for a single rating and average of two independent ratings, respectively. Similarly, for the second observation of a neonate (after an intervention for pain or sedation), the ICC estimates (95% CI) of the pain scale were 0.92 (0.85, 0.96) and 0.96 (0.92, 0.98) for a single rating and average of two independent ratings, respectively. F-tests, carried out to test the null hypothesis that the ICC (single rating) was 0.6 or less (versus >0.6) were highly significant (preintervention $F = 9.65$, $P < 0.0001$ and postintervention $F = 6.36$, $P < 0.0001$).

Sedation scale. The ICC estimates (95% CI) of the first observation of a neonate prior to any intervention for pain or sedation were 0.85 (0.72, 0.92) and 0.92 (0.83, 0.96) for a single rating and average of two independent ratings ($F = 3.06$, $P = 0.001$). The ICC estimates (95% CI) of the second observation of a neonate after an intervention for pain or sedation were 0.90 (0.80, 0.95) and 0.95 (0.89, 0.97) for a single rating and average of two independent ratings ($F = 4.63$, $P < 0.0001$).

Internal consistency analysis

The mean (s.d.) pain scores were 4.9 (3.4) and 5.5 (3.1) for raters 1 and 2, respectively, and the medians (range) were 5 (0, 12) and 5 (0, 12). Cronbach's α for the five-item pain scale was 0.82 and 0.72 for raters 1 and 2, respectively. The mean (s.d.) sedation scores were −2.78 (2.81) and −1.68 (2.23) for raters 1 and 2, respectively and the medians (range) were −2 (−8, 0) and −1 (−8, 0). Cronbach's α for the five-item sedation scale was 0.89 and 0.89 for raters 1 and 2, respectively.

Convergent validity analysis

The correlations between the preintervention N-PASS pain scale and the PIPP were 0.83 and 0.81 for raters 1 and 2, respectively.

Table 2 N-PASS scores by gestational age group

Gestational age (weeks)	*N*[a]	*Mean (prematurity points added)*	*Median*	*s.d.*
>35	12	4.75	5	2.45412
32–35	13	4.7692	4	2.65059
28–31	18	7.1161	6.5	2.68438
<28	13	7.0769	6	2.56455

[a]*N* is larger than sample *N* as some infants were assessed more than once, at varying gestational ages.

Postintervention, the correlations between the N-PASS pain scale and the PIPP were 0.61 and 0.61 for raters 1 and 2, respectively.

Construct validity analysis
The mean (s.d.) preintervention pain score was 4.86 (3.38), which fell to 1.81 (1.53) after analgesic intervention ($P<0.0001$). Similarly, there was a decrease in mean sedation scores from −0.85 (1.66) to −2.78 (2.81) after pharmacologic intervention ($P<0.0001$).

Prematurity points
Table 2 shows the mean preintervention pain scores for each group of premature infants. Scores given include points added for prematurity. The sample size was not sufficient to analyze each group separately.

Discussion

The correlation between the PIPP and the N-PASS was strong, particularly at high pain scores. The correlation was lower for low pain scores, but acceptable, possibly because the PIPP tool assigns a higher score for a quiet infant, while the N-PASS gives a lower score for a quiet infant, resulting in a lower behavior score correlation.

The addition of points to the premature infant's pain score is based upon the research-supported premise that premature infants are less able to exhibit signs of pain than the term infant.[27] Mean scores for each gestational age group are similar without prematurity points added, and therefore may not support the current method of adding points for prematurity. (Table 2) This will be reevaluated following validity and reliability research utilizing the N-PASS with acute-procedural pain. More research is needed on the appropriateness of adding points to the premature infant's score.

Difficulties in behavioral pain assessment and research
Establishing the validity of a behavioral pain and sedation assessment tool is difficult in the absence of a gold standard. Clinically, it is often difficult to interpret the infant's behavior, or determine the etiology of the behavior. A biological marker specifically for pain has not been identified, leaving the clinician with behavioral assessment parameters and clinical judgment to guide management.[1]

Interpretation of the pain and sedation behavior scores within the context of the situation is necessary when utilizing a behavioral pain assessment scoring system.[13] Pain behaviors, exposure to events likely to instigate pain, infant characteristics and health status, presence of other conditions likely to cause distress, such as fatigue, hunger, withdrawal, response to medications and consolability are integrated into pain assessment.[28] Some infants may appear sedated without medication administration, such as septic/lethargic infant or an infant with an abnormal neurological status. Premature infants may also exhibit a 'shut down' reaction to unrelenting or overwhelming pain, and appear sedated.[29] Preterm infants show a heightened motor response to tactile procedures following a painful event.[30] A high degree of suspicion and utilizing preemptive analgesia in known pain situations are important aspects of pain management in any nonverbal population.[13]

Limitations
The N-PASS was studied in the clinical setting rather than by videotaped or laboratory methods due to the goal of developing a clinically usable tool, and the difficulty of videotaping prolonged pain. Bias is unable to be controlled in such a setting. The findings should be interpreted cautiously due to the moderate sample size. The generalizability is limited to one NICU in the Midwest. Further testing is required in other populations and settings and with larger samples to validate our findings.

Further research
The N-PASS tool requires validity and reliability testing with procedural pain and with various nonverbal populations and management styles. Pain assessment of pharmacologically paralyzed and neurologically compromised infants is clinically challenging, requiring further research.

Conclusions
This research provides beginning evidence that the N-PASS is a clinically usable, reliable and valid tool to assess ongoing pain/agitation and sedation in ventilated and/or postoperative infants in the NICU.

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