MedCrave
Step into the World of Research

Journal of Pediatrics & Neonatal Care

Research Article

Open Access

CrossMark

Impacts of a Dexmedetomidine-use guideline on term infants in the NICU: a retrospective and prospective analysis at a single center

Abstract

Introduction: Dexmedetomidine is a non-opioid sedative and analgesic often used in critical care in adults, with potential benefits in decreasing opioid and benzodiazepine use. We implemented a dexmedetomidine-use guideline for analgesia and/or sedation management in a neonatal intensive care unit (NICU) and studied the impact on exposure to opioids, time to full feeds (TFF), and length of hospital stay (LOS).

Methods: Retrospective and prospective chart review studies were completed with term infants admitted to the University of New Mexico Hospital (UNMH) NICU who required continuous infusions for analgesia and/or sedation for management of neonatal encephalopathy (NE) with therapeutic hypothermia treatment. The prospective chart review was conducted following a dexmedetomidine-use guideline implementation, which proposed first-line use of intravenous dexmedetomidine.

Results: Thirty-one infants were included (retrospective: n=13; prospective: n=18 NE). There were no reported adverse events (AEs). In the prospective NE cohort, the LOS decreased from 25 to 17 days (p=0.49), with an increase in the TFF from 5.0 to 10.0 days (p=0.06), although not significant. The opioid exposure significantly decreased in the NE prospective cohort (median exposure in retrospective group 79.00 mcg/kg fentanyl equivalent dose vs 4.02 mcg/kg fentanyl equivalent dose, p<0.001).

Conclusion: The implementation of the dexmedetomidine-use guideline was associated with decreased opioid exposure in term infants with NE. Additional studies are needed to further characterize dexmedetomidine for analgesia and sedation for term infants with other diagnoses.

Keywords: dexmedetomidine, precedex, pediatric pain, infant pain, neonate, sedation, opioid, analgesia

Volume 15 Issue 3 - 2025

Austin Carrier,[1] Elisabeth J Leeflang,[1] Anne Hittson,[1] Zoe Henderson,[2] Dane Winter,[3] Eleni Shenk,[1,4] Jessica M Gross,[5] Jessie R Maxwell[1,6]

[1]Department of Pediatrics, University of New Mexico, USA
[2]School of Medicine, University of New Mexico, USA
[3]School of Medicine, University of California San Diego, USA
[4]Department of Pharmacy, University of New Mexico Hospital, USA
[5]Clinical and Translational Science Center, University of New Mexico, USA
[6]Department of Neurosciences, University of New Mexico, USA

Correspondence: Jessie R. Maxwell, MD, MBA, Associate Professor of Pediatrics and Neurosciences, Department of Pediatrics, Division of Neonatology, University of New Mexico, MSC10 5590; 1 University of New Mexico, Albuquerque, New Mexico, 87131, United States, Tel 505-272-0366, Fax 505-272-1539

Received: October 10, 2025 | **Published:** October 21, 2025

Abbreviations: AE, adverse events; DOL, day of life; IQR, interquartile range; LOS, length of hospital stay; NE, neonatal encephalopathy; NICU, neonatal intensive care unit; NPO, nil per os; TFF, time to full feed; UNM, University of New Mexico; UNMH, University of New Mexico Hospital; US, United States

Introduction

Approximately 9% of infants born in the United States (US) are admitted to a neonatal intensive care unit (NICU)[1] and over 90% of infants in a NICU undergo painful procedures[2] (e.g., heel lances; venipunctures), some experiencing up to 17 painful procedures each day.[3] Contradicting the long-held belief that infants and neonates do not perceive pain,[4,5] current studies show that they can detect, process, and experience pain.[4,6]

Crucial to infants' development, untreated pain and subsequent agitation in the NICU is associated with adverse consequences,[7] including increased blood pressure,[4] hemodynamic instability, pathologic stress response, and inadequate ventilation.[8,9] These adverse events (AEs) increase the risk of both short- and long-term consequences, such as lung injury, changes in hormonal and metabolic levels, and altered behavioral changes, including sleep-wake cycle alterations and irritability,[8] making it imperative to develop safe and effective sedation and pain control in the NICU to support the best outcomes for this population.

Analgesia and sedation in the NICU

Currently, the most commonly used drugs for sedation and pain control in the neonatal population are opioids and benzodiazepines.[2] Although opioids can provide rapid analgesia,[10] they are associated with adverse consequences such as respiratory depression, hypotension, delayed gastric motility, and adverse neurological events (e.g., intraventricular hemorrhage).[11,12] Additionally, midazolam, the most widely used benzodiazepine in neonates, primarily acts as a sedative with little analgesic effect.[13,14] Overall, such side effects from these medications can contribute to increased length of stay in the NICU, infant morbidity and mortality, and cost.[2] A previous retrospective review found that exposure to fentanyl, midazolam, or morphine in very low birth weight infants (<1,500 grams at birth) was independently predictive of discharge with gastrostomy tube feedings.[15] These medications remain the most commonly used due to a lack of evidential support for alternatives,[15] demonstrating the need for further investigation into other therapeutic options.

Dexmedetomidine as an alternative treatment

Dexmedetomidine (trade name Precedex™) is a non-opioid alternative for analgesia and sedation.[16] Despite limited pharmacokinetic data in infants and no large randomized controlled clinical trials, dexmedetomidine is becoming an increasingly commonly used alternative for pain and agitation management in neonates.[2,16,17]

Dexmedetomidine is a highly selective centrally acting alpha 2-adrenergic agonist, currently approved by the US Food and Drug Administration for use in non-intubated adults for procedural or surgical sedation less than 24 hours.[2,18] Dexmedetomidine acts in multiple locations throughout the central nervous system, though its sedative and anxiolytic effects are primarily a result of its activity in the locus coeruleus of the brainstem. In this area, alpha 2-adrenergic receptors are stimulated, reducing central sympathetic output and resulting in increased firing of inhibitory neurons.[19] Thus, dexmedetomidine can provide both sedation and analgesia.[16]

Because of its characteristics, dexmedetomidine has significant advantages as a procedural sedative. It has a relatively short half-life and lacks the respiratory depressant effects observed in opioids and benzodiazepines. For these reasons, it is a useful tool for management in pediatric populations.[19,20] Many NICUs across the United States have implemented guidelines for routine use of dexmedetomidine rather than midazolam, fentanyl, and/or morphine.[21] Recent studies showed that the use of dexmedetomidine resulted in a reduction in dose or discontinuation of other sedative agents.[19,20,22] Additionally, while studies in the neonatal population remain scarce, some studies have demonstrated low incident and severity of adverse consequences when utilizing low starting doses that are gradually increased to minimize adverse reactions.[23,24] Specifically, clearance of dexmedetomidine is slower in neonates than older children, with a longer half-live observed in neonates than in older children.[25] This is even more pronounced at lower gestational ages.[2,26,27] Thus, intravenous doses of 0.3-0.5 mcg/kg/hour are often effective in surgical adult patients, while neonatal patients may only require 0.1-0.2 mcg/kg/hour.[16]

Neonatal encephalopathy

Neonatal encephalopathy (NE) involves a significant perinatal event that generates hypoxic-ischemic injury with often neurodevelopmental and end-organ sequelae.[28] NE occurs in up to 3 per 1,000 live births, and is the leading contributor to neurodevelopmental disability worldwide.[29] NE is categorized as mild, moderate, or severe by clinical examination. Moderate to severe NE is treated with whole-body therapeutic hypothermia (TH) within 6 hours of birth to mitigate neurodevelopmental impairment; however, TH dysregulates normal homeostasis resulting in additional stress to the body and brain if not managed with analgesia and sedation.[30,31]

Opioids and benzodiazepines compound these deleterious effects on the developing brain through multiple mechanisms. Infants may also require intubation and sedation for poor respiratory drive or seizures secondary to NE. There is wide variation currently in clinical practice due to a lack of standardized practice recommendations or guidelines for analgesia and sedation strategies in neonates undergoing TH, and insufficient data on the long-term neurologic outcomes after exposure to these regimens.[31,32] While the long-term effects of dexmedetomidine exposure on brain injury and maturation in term infants are currently not well characterized,[33] new data comparing dexmedetomidine to morphine supported dexmedetomidine as a first-line sedation agent during TH.[24,29]

Based on the known mechanism of dexmedetomidine and its success in treating term infants, we proposed a chart review study (retrospective and prospective) to determine if the implementation of a dexmedetomidine-use guideline for analgesia and sedation management in the University of New Mexico Hospital (UNMH) NICU would reduce exposure to opioids while observing the frequency of adverse events (AEs, i.e., events of hemodynamic instability), time to full feed (TFF), and length of hospital stay (LOS) in a population undergoing TH treatment. We hypothesized that implementation of the guideline in term infants would correlate with a reduced exposure of opioids, decreased AEs, decreased TFF, and decreased LOS.

Materials and methods

Following approval from the University of New Mexico (UNM) Institutional Review Board, a two-part chart review study was completed at the Level IV UNMH NICU. Eligible term infants (≥37 weeks' gestation) with neonatal encephalopathy (NE) requiring therapeutic hypothermia treatment during both time reviews were included. Infants born preterm (<37 weeks' gestation) or those without a NE diagnosis requiring therapeutic hypothermia were excluded from the reviews. Information was collected for each infant as to any sedative or analgesic medication administered, including continuous infusions. Data were collected from the date of the NICU admission to discharge or transfer from the NICU. Only IRB-approved study team members conducted the chart reviews.

Retrospective chart review

The retrospective chart review (November 1, 2019 through November 1, 2021) collected baseline data, including gestational age, sex, mode of delivery, indication for medication), type of sedation and/or analgesic medication administered (i.e., opioid; benzodiazepine; dexmedetomidine), day of life (DOL) medication was started, duration (in days) on medication, duration infant was *nil per os* (NPO) and TFF following medication exposure, any requirement to transition from intravenous to enteral administration of sedation/analgesic medication, AEs (i.e., events of hemodynamic instability including bradycardia, hypotension or hypertension defined based on gestational age), LOS, and outcome at time of discharge. These data provided a baseline for courses of hospital stays and local practice of pain management and sedation in the NICU.

Dexmedetomidine-use guideline

A dexmedetomidine-use guideline was developed based on current available literature[7,20,34] in collaboration between neonatology and pediatric clinical pharmacists, and was implemented on August 1, 2022, in the UNMH NICU (see Table 1). The guideline proposed the use of intravenous dexmedetomidine at the time of NICU admission as standard of care for hemodynamically stable term infants with a diagnosis of NE requiring sedation for whole-body hypothermia treatment. A loading dose of 1 mcg/kg could be administered if the infant had stable blood pressure and heart rate, followed by continuous infusion at 0.1 mcg/kg/hour. The dose was increased by 0.1 mcg/kg/hr every 2 hours as clinically indicated to a maximum dose of 0.5 mcg/kg/hr. Once ready to wean, the dose was decreased by 0.1 mcg/kg/hr every 12 to 24 hours and discontinued completely once the infusion rate was 0.1 mcg/kg/hr (Table 1). The guideline outlined safe and appropriate dosing initiation, maintenance, and a weaning protocol based on infant weight and continued infant stability. Additionally, the guideline proposed the consideration of opioids (i.e., fentanyl or morphine) as a second-line treatment or if acute relief was indicated. Appropriate education regarding dosing, maintenance, and weaning were provided to NICU providers before the implementation of the guideline.

Prospective chart review

A prospective chart review was conducted on eligible NICU patients (August 1, 2022, through June 30, 2023) after the dexmedetomidine guideline was introduced. The same data were

Citation: Carrier A, Leeflang EJ, Hittson A, et al. Impacts of a Dexmedetomidine-use guideline on term infants in the NICU: a retrospective and prospective analysis at a single center. *J Pediatr Neonatal Care*. 2025;15(3):152–157. DOI: 10.15406/jpnc.2025.15.00601

collected as during the retrospective chart review. These data provided information on courses of hospital stays and local practice of pain management and sedation in the NICU following the implementation of the dexmedetomidine-use guideline.

Table 1 Dexmedetomidine algorithm: University of New Mexico

Consideration for dexmedetomidine initiation
Consider initiating intravenous Dexmedetomidine for the following patient population at time of admission as standard of care:
(i) Term infant (≥37 weeks' gestation).
(ii) Diagnosis of neonatal encephalopathy and requiring whole body hypothermia treatment.
Dexmedetomidine initiation – weight based
Loading dose may be considered in infants that are hemodynamically stable at 1 mcg/kg to run over 10-20 minutes:
(i) Starting dose of intravenous dexmedetomidine hydrochloride (4 mcg/mL) at 0.1 mcg/kg/hour using birth weight for dosing weight.
(ii) Monitor vital signs closely including blood pressure (q 15 minutes x1 hour) when initiating the drip.
Dexmedetomidine maintenance / escalation
Escalate dose if care team determines that infant is not adequately sedated:
(i) Increase baseline dose by 0.1 mcg/kg/hr q2 hours.
(ii) May increase dose no faster than every 30 minutes if infant tolerates increase and vitals remain stable.
(iii) Consider use of PRN morphine intravenous dosing if acute relief is indicated.
(iv) Maximum recommended dose is: 0.5 mcg/kg/hr.
(v) Continue to closely monitor vital signs including blood pressure (q 15 minutes x1 hour) and heart rate when titrating the dose.
(vi) Consider use of fentanyl or morphine for second line medications when indicated.
Dexmedetomidine weaning
Once the infant is stabilized and sedation is no longer needed, begin weaning:
(i) Wean by 0.1 mcg/kg/hr every 12-24 hours as tolerated.
(ii) Discontinue dexmedetomidine when dose is 0.1 mcg/kg/hr.

References

McPherson C, et al. Seminars in Fetal and Neonatal Medicine, 2021

Morton SU, et al. Pediatrics, 2021

Analysis

Descriptive statistics were used to summarize the characteristics of the full retrospective and prospective samples. Continuous variables, which were not normally distributed, are reported as medians with interquartile ranges (IQR). Categorical variables, including sex and mode of delivery, are presented as counts and percentages. Comparative analyses between retrospective and prospective samples for each cohort as well as the combined cohorts were conducted using the appropriate statistical test for the type of variable. For continuous variables, we used the Mann-Whitney U test, and for categorical variables, we used Fisher's exact tests. Multivariate Kruskal-Wallis tests were used to further examine whether the retrospective and prospective samples differ for any of the following outcomes:

1) Number of days requiring medication,
2) LOS, and
3) TFF.

We first converted the morphine doses to an equivalent fentanyl dose to compare all opioid exposure in the groups for morphine and fentanyl use. The equivalent fentanyl dose was used as this was the most commonly used opioid. This was calculated by taking the cumulative morphine dose (in mg/kg for a 24-hour period) and dividing the value by 6 to provide the dose of intravenous morphine in mg/kg/dose that would be given every 4 hours. That dose was then multiplied by 10 to get the equivalent dose of intravenous fentanyl (mcg/kg/hr). The dose was multiplied by 24 to obtain the converted intravenous fentanyl dose in mcg/kg. The analysis was then completed via assessing the normality of opioid and benzodiazepine exposure within each group using Shapiro-Wilk tests. Given the violation of normality, we evaluated differences in exposure between the retrospective and prospective groups using Wilcoxon rank sum tests. To examine differences in feed types between the retrospective and prospective groups, we used Fisher's exact tests, as the small sample sizes in some groups were not appropriate for a chi-square test.

All analyses were performed using R 4.3.3. P-values were adjusted for multiplicity using the Benjamini-Hochberg method, and adjusted values < 0.05 were considered significant. We provide these adjusted p-values in the results.

Results

Thirty-one infants with NE were included in the analysis for this study: 13 infants in the retrospective chart review and 18 infants in the prospective chart review. Clinical and demographic characteristics are described in Table 2. All 18 infants in the prospective chart review received dexmedetomidine as the first-line sedation and analgesia medication. The median DOL sedation or analgesia medication was started significantly earlier in the prospective cohort (IQR, retrospective 0.0 [0.0-1.0] versus prospective 0.0 [0.0-0.0]; $p<0.05$). The length of sedation or analgesia medication administration decreased in the prospective cohort compared to the retrospective, although not significantly (IQR, retrospective 7.0 [4.0-11.0] versus prospective 6.0 [5.0-6.0]; $p=0.52$). There were trends towards a decreased median LOS (25 to 17 days [$p=0.49$]) and increased TFF (5 to 10 days [$p=0.06$]) in the prospective cohort, however these were not significant.

Table 2 Clinical and demographic characteristics of infants with neonatal encephalopathy

Characteristic	All	Retrospective	Prospective	Adjusted p value[†]
n	31	13	18	-
Sex	*n (%)*			
Female	14 (45.2)	5 (38.5)	9 (50)	0.84
Male	17 (54.8)	8 (61.5)	9 (50)	
Mode of Delivery				
Cesarean	17 (54.8)	10 (77.0)	7 (38.9)	0.25
Vaginal	14 (45.2)	3 (23.0)	11 (61.1)	
	median (IQR)			
Gestational age at birth (weeks)	39.0 (37.2 - 40.0)	39.3 (39.0 - 40.0)	38.7 (37.0-39.9)	0.5
Fentanyl equivalent dose (mcg/kg)		79.0 (61.1 - 523.7)	4.0 (0.0 - 7.0)	0
DoI medication started	0.0 (0.0 - 0.0)	0.0 (0.0 - 1.0)	0.0 (0.0 - 0.0)	0.14
Length of medication administration^ (days)	6.0 (4.0 - 7.0)	7.0 (4.0 - 11.0)	6.0 (5.0 - 6.0)	0.73
Time NPO during medication administration^ (days)	5.0 (4.0 - 6.0)	5.0 (4.0 - 7.0)	6.0 (5.0 - 6.0)	0.84
TFF after medication exposure^ (days)	8.0 (6.5 - 11.0)	5.0 (5.0 - 8.0)	10.0 (8.0 - 11.8)	0.06
LOS (days)	17.0 (11.5 - 27.0)	25.0 (13.0 - 27.0)	17.0 (10.2 - 24.8)	0.49

[†]p-values adjusted for multiplicity using the Benjamini-Hochberg method

^Medication is defined as any sedative or analgesic used intermittently or via continuous infusion

Opioid and benzodiazepine exposure

For the retrospective NE group (n=13), the median total exposure was 79.00 mcg/kg fentanyl equivalent dose (IQR, 61.07-523.65 mcg/kg fentanyl equivalent dose). In contrast, the prospective NE group (n=18) had a median exposure of 4.02 mcg/kg fentanyl equivalent dose (IQR, 0.00 - 7.00 mcg/kg fentanyl equivalent dose).

This difference was statistically significant (p=0.00). The rank-biserial correlation was -0.83, indicating a large decrease in exposure in the prospective group relative to the retrospective group.

Multivariate analysis

Medians, IQRs, and p-values for the Fisher's exact and Mann-Whitney U tests for demographic and clinical variables are provided in Table 1. After adjusting for multiple tests, the TFF differed significantly between the cohorts with the prospective sample tending to have longer times to full feeds than the retrospective sample (p=0.03). The multivariate Kruskal-Wallis tests showed significant differences in the TFF (p=0.01). Infants in the prospective sample tended to have longer times to full feeds than infants in the retrospective sample.

Discussion

Analgesia and sedation in the NICU have historically been controversial due to the concern of short- and long-term adverse consequences within this vulnerable population, lack of sufficient pharmacokinetic data within this population, and challenges with pain assessment as the gold-standard of pain assessment tools generally rely on patient self-report.[5,7,35] This difficulty in pain assessment is further complicated by evidence suggesting that preterm infants may experience pain more intensely than their term counterparts. Some studies indicate that preterm infants are potentially more hypersensitive due to the higher density of nociceptive nerve endings in their skin, along with immature development of inhibitory pain control,[4,36] further hindering their ability to modulate and manage pain.

Currently, few studies demonstrate the safety and efficacy of dexmedetomidine use within the NICU population. There are well-established adverse consequences of opioid exposure in the neonatal and infant population, and dexmedetomidine potentially offers considerable benefits over the present standard of care using opioids and benzodiazepines. Within our population, we were able to decrease the exposure to opioids and/or benzodiazepines for infants requiring hypothermia treatment with NE with no observed AEs.

The delay to reaching full feeds is interesting and may either represent more medically complex infants in the prospective cohort or possibly increased use of mother's own milk. The hospital advocates for use of mother's own milk and works to support establishing breastfeeding or breastmilk whenever possible. Perceived stress, a common finding in individuals with an infant in the NICU, is linked to nonoptimal breastfeeding outcomes.[37,38]

Additionally, psychosocial stress has been observed to negatively affect energy density and fat content of mother's own milk,[39] which may prolong the time to reach full volume feeds with appropriate growth.

Study strengths

Demonstrating reduced opioid exposure in this vulnerable NE population following the guideline implementation is a considerable strength in this study. Furthermore, as there were no reported AEs or intolerance of dexmedetomidine following the implementation of the guideline, this study lays the groundwork for dexmedetomidine as a potentially safe alternative for analgesia and sedation, although additional studies are required. Much of the hesitation of supplanting opioids with alternative treatments like dexmedetomidine is the lack of sufficient pharmacokinetic and clinical data within this population and additional information is needed on the possible impact on neurodevelopmental outcomes. Thus, additional studies investigating the safety, efficacy, and developmental outcomes of infants exposed to dexmedetomidine are needed to close the gaps in medicinal knowledge.

Study limitations

There are limitations to this study, including 1) relatively small sample sizes and 2) limitation to one study site. Due to the small sample size, the results of the study may not be generalizable to the wider NICU population of term infants. The small sample size limited

the study's power to detect significant effects across cohorts, as seen in our results.

Conclusion

We demonstrated that the implementation of a dexmedetomidine-use guideline within a NICU was associated with a reduced opioid exposure in term infants who required hypothermia treatment for NE diagnosis. Successful creation and implementation of the guideline was contingent on an interdisciplinary team and adequate training to providers within the care setting. Importantly for future work investigating its safety and efficacy, no AEs (i.e., hemodynamic instability) were reported following the implementation of dexmedetomidine. Due to limitations of small sample sizes and diagnostic heterogeneity, additional studies with adequate and matched sample sizes are needed to determine the safety and efficacy of dexmedetomidine for analgesia and sedation within the NICU.

Acknowledgments

The authors would like to thank all the providers, pharmacists, and nurses at the University of New Mexico Neonatal Intensive Care Unit for their assistance.

The authors are grateful for the support received from the Department of Pediatrics and the Division of Neonatology. Dr. Gross' bio statistical consultation was supported through This project is supported by an award from the National Institutes of Health (NIH) under grant number UL1TR001449 and/or KL2TR001448.

Funding

None.

Conflicts of interest

The authors declare no conflicts or financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employment, gifts, and honoraria. The authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

References

1. Kim Y, Ganduglia-Cazaban C, Chan W, et al. Trends in neonatal intensive care unit admissions by race/ethnicity in the United States, 2008-2018. *Sci Rep*. 2021;11(1):23795.
2. Greenberg RG, Wu H, Laughon M, et al. Population pharmacokinetics of dexmedetomidine in infants. *J Clin Pharmacol*. 2017;57(9):1174–1182.
3. Assefa E, Dinkiye M, Geleta T, et al. The practice of procedural pain assessment and management in neonatal intensive care unit in Ethiopia: cross-sectional study. *Health Sci Rep*. 2022;5(2):e533.
4. Anand KJ, Hickey PR. Pain and its effects in the human neonate and fetus. *N Engl J Med*. 1987;317(21):1321–1329.
5. Hall RW. Anesthesia and analgesia in the NICU. *Clin Perinatol*. 2012;39(1):239–254.
6. Perry M, Tan Z, Chen J, et al. Neonatal pain: perceptions and current practice. *Crit Care Nurs Clin North Am*. 2018;30(4):549–561.
7. McPherson C, Miller SP, El-Dib M, et al. The influence of pain, agitation, and their management on the immature brain. *Pediatr Res*. 2020;88(2):168–175.
8. Bhalla T, Shepherd E, Tobias JD. Neonatal pain management. *Saudi J Anaesth*. 2014;8(Suppl 1):S89–S97.
9. Dix LML, Shepherd K, Polglase GR, et al. The cerebral hemodynamic response to pain in preterm infants with fetal growth restriction. *Front Pediatr*. 2020;8:268.
10. Anand KJ, Hall RW. Pharmacological therapy for analgesia and sedation in the newborn. *Arch Dis Child Fetal Neonatal Ed*. 2006;91(6):F448–F453.
11. Hall RW, Shbarou RM. Drugs of choice for sedation and analgesia in the neonatal ICU. *Clin Perinatol*. 2009;36(2):215–226.
12. Pacifici GM. Clinical pharmacology of fentanyl in preterm infants. a review. *Pediatr Neonatol*. 2015;56(3):143–148.
13. Committee on fetus and newborn section on anesthesiology and pain medicine. Prevention and management of procedural pain in the neonate: an update. *Pediatrics*. 2016;137(2):e20154271.
14. Pacifici GM. Clinical pharmacology of midazolam in neonates and children: effect of disease-a review. Int J Pediatr. 2014;2014:309342.
15. Astoria MT, Thacker L, Hendricks-Munoz KD. Oral feeding outcome after analgesic and sedative exposure in VLBW preterm infant. *Am J Perinatol*. 2018;35(14):1399–1404.
16. Mantecon-Fernandez L, Lareu-Vidal S, Gonzalez-Lopez C, et al. Dexmedetomidine: an alternative to pain treatment in neonatology. *Children (Basel)*. 2023;10(3):454.
17. Curtis S, Kilpatrick R, Billimoria ZC, et al. Use of dexmedetomidine and opioids in hospitalized preterm infants. *JAMA Netw Open*. 2023;6(11):e2341033.
18. McDonald D, Palsgraf H, Shah P. Dexmedetomidine - an emerging option for sedation in neonatal patients. *J Perinatol*. 2022;42(7):845–855.
19. Buck ML. Dexmedetomidine use in pediatric intensive care and procedural sedation. *J Pediatr Pharmacol Ther*. 2010;15(1):17–29.
20. Morton SU, Labrecque M, Moline M, et al. Reducing benzodiazepine exposure by instituting a guideline for dexmedetomidine usage in the NICU. *Pediatrics*. 2021;148(5):e2020041566.
21. Stark A, Smith PB, Hornik CP, et al. Medication use in the neonatal intensive care unit and changes from 2010 to 2018. J *Pediatr*. 2022;240:66–71.e4.
22. Squillaro A, Mahdi EM, Tran Net al. Managing procedural pain in the neonate using an opioid-sparing approach. *Clin Ther*. 2019;41(9):1701–1713.
23. Zuppa AF, Nicolson SC, Wilder NS, et al. Results of a phase 1 multicentre investigation of dexmedetomidine bolus and infusion in corrective infant cardiac surgery. *Br J Anaesth*. 2019;123(6):839–852.
24. Cosnahan AS, Angert RM, Jano E, et al. Dexmedetomidine versus intermittent morphine for sedation of neonates with encephalopathy undergoing therapeutic hypothermia. *J Perinatol.* 2021;41(9):2284–2291.
25. Chrysostomou C, Schulman SR, Herrera Castellanos M, et al. A phase II/III, multicenter, safety, efficacy, and pharmacokinetic study of dexmedetomidine in preterm and term neonates. *J Pediatr*. 2014;164(2):276–282.e1–3.
26. McAdams RM, Pak D, Lalovic B, et al. Dexmedetomidine pharmacokinetics in neonates with hypoxic-ischemic encephalopathy receiving hypothermia. *Anesthesiol Res Pract*. 2020;2020:2582965.
27. Zimmerman KO, Wu H, Laughon M, et al. Dexmedetomidine pharmacokinetics and a new dosing paradigm in infants supported with cardiopulmonary bypass. *Anesth Analg*. 2019;129(6):1519–1528.
28. Jumani T, Mishra P, Robinson T, et al. Short-term effects of opioids during therapeutic hypothermia for neonatal encephalopathy. *Front Pediatr*. 2024;12:1405731.

29. Nuzum TA, Kazmi SH, Wachtel EV. The effect of using dexmedetomidine versus morphine as sedation on long-term neurodevelopmental outcomes of encephalopathic neonates undergoing therapeutic hypothermia. *J Perinatol*. 2025;45(8):1081–1086.

30. Elliott M, Burnsed J, Heinan K, et al. Effect of dexmedetomidine on heart rate in neonates with hypoxic ischemic encephalopathy undergoing therapeutic hypothermia. *J Neonatal Perinatal Med*. 2022;15(1):47–54.

31. Joshi M, Muneer J, Mbuagbaw L, et al. Analgesia and sedation strategies in neonates undergoing whole-body therapeutic hypothermia: a scoping review. *PLoS One*. 2023;18(12):e0291170.

32. McPherson C, Frymoyer A, Ortinau CM, et al. Management of comfort and sedation in neonates with neonatal encephalopathy treated with therapeutic hypothermia. *Semin Fetal Neonatal Med*. 2021;26(4):101264.

33. Selvanathan T, Miller SP. Effects of pain, sedation and analgesia on neonatal brain injury and brain development. *Semin Perinatol*. 2024;48(5):151928.

34. McPherson C, Grunau RE. Pharmacologic analgesia and sedation in neonates. *Clin Perinatol*. 2022;49(1):243–265.

35. Gregory J. Use of pain scales and observational pain assessment tools in hospital settings. *Nurs Stand*. 2019;40(10).

36. Fitzgerald M, Beggs S. The neurobiology of pain: developmental aspects. *Neuroscientist*. 2001;7(3):246–257.

37. Nagel EM, Howland MA, Pando C, et al. Maternal psychological distress and lactation and breastfeeding outcomes: a narrative review. *Clin Ther*. 2022;44(2):215–227.

38. Fernandez-Vaz C, Gonzalez-Sanz JD. Cortisol, maternal stress, and breastfeeding rate at hospital discharge: a systematic review. *Breastfeed Med*. 2022;17(12):984–993.

39. Ziomkiewicz A, Babiszewska M, Apanasewicz A, et al. Psychosocial stress and cortisol stress reactivity predict breast milk composition. *Sci Rep*. 2021;11(1):11576.

Citation: Carrier A, Leeflang EJ, Hittson A, et al. Impacts of a Dexmedetomidine-use guideline on term infants in the NICU: a retrospective and prospective analysis at a single center. *J Pediatr Neonatal Care*. 2025;15(3):152–157. DOI: 10.15406/jpnc.2025.15.00601