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Brief Report

Opioid Infusions in the Neonatal Intensive Care Unit

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OBJECTIVES The primary objective of this study was to compare the use of opioid infusions to that proposed in guidelines published in an in-house medication handbook. Secondary objectives were to assess the documented use of a standardized neonatal pain assessment tool and to describe the supplemental use of opioids concurrent with an opioid infusion.
METHODS A retrospective chart review was performed for all patients in the NICU who received opioid infusions between November 1, 2005, and November 30, 2006. Data collected included patient characteristics, opioid infusion dosing and duration, supplemental opioid use, and pain assessment documentation.
RESULTS Of the110 neonates who received morphine or fentanyl during the study period, 65 patients met inclusion criteria. Reasons for starting an opioid infusion included nonsurgical sedation and/or analgesia (51%), postoperative pain (17%), and procedural pain (1%). No reason was documented for 31% of patients. Thirty-eight percent of neonates received a loading dose of opioid before initiation of the infusion. The median dose was 100 mcg/kg (IQR=48.2) for morphine and and 1 mcg/kg (IQR=0.8) for fentanyl. The mean ± SD starting rates of morphine and fentanyl infusions were 12.3 ± 4.7 mcg/kg/hr and 1.5 ± 1.7 mcg/kg/hr, respectively. Supplemental opioid doses were given to 46% of neonates during the infusion period. Supplemental doses were given for procedures (69%) and pain/agitation/sedation (26%). No reason was documented for 5% of patients. The Neonatal Pain, Agitation and Sedation Scale scores were only documented 9% of the time for each day that the patient received an opioid infusion.
CONCLUSIONS Dosing of opioids generally was within the recommendations that are described in the in-house medication handbook. A substantial percentage of neonates received supplemental opioid doses while on opioid infusions, mostly for procedural pain management. Documentation of the reason for using opioid infusions and the assessment of neonatal pain was poor.

KEYWORDS analgesics, infants, intensive care units, newborn, neonate, opioid

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INTRODUCTION

The importance of neonatal pain management has become increasingly recognized in recent years. As little as 20 years ago, it was a common opinion among physicians that neonates were incapable of feeling pain. Even physicians who acknowledged that neonates likely experience some degree of pain were hesitant to use analgesics in this population because of concerns about addiction and side effects.[1,2] As a result, adequate analgesia was seldom achieved during neonatal surgeries and procedures.

ABBREVIATIONS IQR, interquartile range; NICU, neonatal intensive care unit; N-PASS, Neonatal Pain, Agitation, and Sedation Scale; SJHC, St. Joseph's Heath Care

Over the last two decades, much research has been conducted on the topic of neonatal pain, and today it is understood that neonates not only experience pain, but that the short- and long-

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Table 1. Dosing Recommendations per SJHC NICU Medication Handbook*[12]

	Type of Infusion	
	Morphine (IV)	**Fentanyl (IV)**
Intermittent dosing	50 to 200 mcg/kg	1 mcg/kg (<1500g) 2 mcg/kg (>1500g)
Continuous infusion	10 to 20 mcg/kg/hr (usual range)	1 to 5 mcg/kg/hr (usual range)
Weaning from continuous infusion	Decrease by 10% per day to 1-2 mcg/kg/hr then discontinue	Decrease by 10% per day to 1 mcg/kg/hr, then: 1 mcg/kg IV q 4hr for 24 hr, then 1 mcg/kg IV q 6hr for 24hr, then 1 mcg/kg IV q 8hr for 24 hr, then 1 mcg/kg IV q 12hr for 24hr, then discontinue

**IV indicates intravenous administration*

term consequences of inadequately treated pain can include physiological compromise, altered brain development, and behavioural effects.[3-7] Consensus statements from various pediatric groups urge healthcare practitioners to acknowledge and recognize sources of neonatal pain and to adopt evidence-based practice guidelines for neonatal pain management.[8-11] Common to all of these guidelines are the recommendation that an effective approach must include the prevention and/or limitation of exposure to painful stimuli; the assessment of neonatal pain by standardized, validated, and reliable scoring tools; and the treatment of pain using nonpharmacological and pharmacological methods. Although many of the recommendations are related to short-term procedural pain management, the guidelines also include recommendations for the management of long-term pain, such as postoperative pain.

St. Joseph's Heath Care (SJHC) in London, Ontario, Canada, has adopted guidelines to support the practice of neonatal pain management. The hospital's neonatal intensive care unit (NICU) medication handbook outlines recommendations for dosing narcotic analgesics, including intermittent and continuous dosing as well as recommendations for weaning patients from continuous opioid infusions (Table 1).[12] The Neonatal Pain, Agitation and Sedation Scale (N-PASS) was developed by practitioners at Loyola University Health System, Loyola University, Chicago, IL (see www.n-pass.com). In May 2005, our hospital introduced the N-PASS as a standardized neonatal pain assessment tool[13] and recommended that the N-PASS be calculated and documented for every patient in the NICU at least every 12 hours and more frequently for patients who were receiving analgesics.

The primary objective of this study was to compare the use of opioid infusions to use guidelines that are published in an in-house medication handbook. Secondary objectives were to assess the documented use of a standardized neonatal pain assessment tool and to describe the supplemental use of opioids concurrent with an opioid infusion.

MATERIALS AND METHODS

A retrospective chart review was performed for all patients in the NICU who received opioid infusions between November 1, 2005, and November 30, 2006. We used the NICU database to identify patients who received either morphine or fentanyl. Patients were excluded if they did not receive an opioid infusion (i.e., received bolus doses only), if they were born to opioid-dependent mothers, or if they were transferred to SJHC from another hospital. Only the first opioid infusion was included in analysis for any infant who received multiple infusions of opioids during hospitalization. This was done because opioid requirements after repeated infusions would likely be dependent on prior exposure; hence, the usual dosing recommendations may not have applied to these patients. Data collection included patient characteristics, opioid infusions, supplemental opioid use, and N-PASS documentation.

Data were analyzed with the statistical software package SPSS, version 14.0. Percentages

Table 2. Patient Characteristics (n=65)

Gestational age, wk*	31 ± 5
Birth weight, kg*	1.62 ± 0.98
NICU length of stay, days*	60 ± 45
Male, No. (%)	35 (55)

**mean ± SD except where noted*

were used to summarize categorical variables. Normally distributed continuous variables were described as mean and standard deviation, and skewed continuous variables were described as median and interquartile range (IQR).

RESULTS

Of the 110 neonates identified as having received morphine or fentanyl at admission, 38 received bolus doses only, 4 were born to opioid-dependent mothers, and 2 were transferred to SJHC from another hospital, and were therefore excluded. On review, one case was found to be highly complicated and included the use of an ultra low-dose naloxone infusion. It was subsequently decided to exclude this case from the final analysis since it represented a substantial deviation from usual practice. Thus, 65 patients were included in our study.

Patient characteristics are presented in Table 2. Fifty-one percent of opioid infusions were documented as being used for nonsurgical-related sedation, analgesia, or both. Postoperative pain (17%) and procedural pain (1%) were documented as reasons for starting opioid infusions. A reason for starting opioid infusion was not documented for nearly one-third (31%) of patients. Table 3 details the reasons for starting an opioid infusion.

Morphine infusions were used in 80% of the patients; fentanyl infusions were used in the remaining 20% (Table 4). Thirty-eight percent of the neonates received a loading dose of opioid before the beginning of the infusion, with the median dose being 100 mcg/kg (IQR=48.2) for morphine and 1 mcg/kg (IQR=0.8) for fentanyl. The mean infusion starting rates were 12.3 ± 4.7 mcg/kg/hr for morphine and 1.5 ± 1.7 mcg/kg/hr for fentanyl. The combined median duration of infusion was 7 days (IQR=10.4). The median tapering duration was 3.5 days (IQR=6.3).

Supplemental doses of opioid were given to 46% of neonates during the infusion period (Table 5). On average, patients received a median of 1 dose (IQR=2) of supplemental opioid during an opioid infusion. Reasons documented for giving supplemental doses were procedures (69%) and pain/agitation/sedation (26%). No reason was documented in 5% of cases.

Table 3. Reasons for Starting Opioid Infusion

Reason	No. (%)
Nonsurgical-related sedation and/or analgesia	
Sedation	11 (17)
Agitation	5 (8)
Irritability	4 (6)
Sedation and analgesia	4 (6)
Analgesia	2 (3)
Poor respiration	2 (3)
Painful disease state due to NEC	2 (3)
Pain management other than for NEC	1 (1)
Discomfort during prolonged intubation	1 (1)
Discomfort not related to prolonged intubation	1 (1)
Total	33 (51)
Not stated	20 (31)
Postoperative analgesia	
PDA ligation	6 (9)
Omphalocele repair	2 (3)
Gastroschisis repair	2 (3)
Repair of esophageal atresia	1 (1)
Total	11 (17)
Procedural pain due to chest tube insertion	1 (1)

Although most (77%) patients had at least 1 N-PASS documented during the infusion period, only 9% had a documented N-PASS for each day while receiving an opioid infusion. The median ratio of number of days with at least 1 documented N-PASS compared with total infusion duration was 0.3 (IQR=0.46).

DISCUSSION

With an increased awareness in recent years of the importance of neonatal pain management, SJHC has developed guidelines to support practitioners in treating and assessing neonatal pain. Our results suggest that bolus and infusion dosing of morphine and fentanyl generally fall within the recommendations outlined in the

Table 4. Infusion Descriptives

	Type of Infusion		
	Morphine	**Fentanyl**	**Total**
Opioid used, No. (%)	52 (80)	13 (20)	65 (100)
Loading dose given, No. (%)	21 (40)	4 (31)	25 (38)
Loading dose, mcg/kg	100 (48)	1.0 (0.8)	N/A
Infusion rates, mcg/kg/hr			
Starting rate†	12.3 ± 4.7	1.5 ± 0.7	N/A
Peak rate†	19.5 ± 8.7	3.1 ± 1.6	N/A
Final rate at discontinuation*	2.1 (5.5)	0.6 (1.5)	N/A
Infusion times, days			
Time to peak dose*	0.125 (0.81)	0.83 (4.6)	0.125 (1.3)
Duration at peak dose*	2.0 (2.7)	1.1 (3.5)	2.0 (2.7)
Duration of taper*	3.7 (6.5)	3.0 (5.2)	3.5 (6.3)
Total infusion duration*	6.9 (10.9)	7.5 (13.2)	7.0 (10.4)

NA, Not available
**Values expressed as median (interquartile range) except where noted*
†Values expressed as mean ± SD

SJHC NICU medication handbook. Indications for starting an opioid infusion were poorly documented. Medical records for 31% of patients did not have a documented reason for starting the infusion, and the reason was vaguely stated in the records of the 43% of patients whose records included a reason. For example, it was fairly common for a progress note to include a statement such as "morphine infusion started for analgesia," with no further description about the source of pain or reason analgesia was needed. In contrast, reasons for giving supplemental doses of opioid during the infusion were well documented (Table 5), with no reason documented for only 5% of patients. Furthermore, reasons for giving the dose were often well specified. For example, "morphine 100 mcg/kg for chest tube insertion" was commonly stated. Documentation was written in multiple areas of the chart, including physician orders, progress notes, and nursing flow sheets.

Documentation of neonatal pain assessment in the form of the N-PASS was infrequent, despite guidelines suggesting a score be calculated and documented at least every 12 hours. Only 9% of neonates received at least one score each day during the infusion period, and 23% of neonates had absolutely no N-PASS documentation during the entire infusion period. To improve and optimize neonatal pain management, a standardized, objective, and consistent method of documenting neonatal pain is necessary.

Table 5. Supplemental Opioid Use During an Opioid Infusion*

Neonates receiving supplemental opioid doses	30 (46)
Average number of doses given, median (IQR)	1 (2)
Reason dose given	
Procedure	45 (69)
Pain/agitation/sedation	17 (26)
Not stated	3 (5)

IQR, interquartile range; No., number
**Values expressed as No. (%) except where noted.*

CONCLUSIONS

Our results show that dosing of opioids at SJHC generally falls within the recommendations in the SJHC NICU Medication Handbook. A substantial percentage of neonates receive supplemental opioid doses while on opioid infusions, mostly for procedural pain management. Given the retrospective nature of our study and because documentation of indications for using opioid infusions and of assessment of neonatal pain was poor, it is not possible for us to assess effectiveness of current practice in neonatal pain management. We recommend that documentation practices be improved in order to better support optimal clinical management of neonatal pain.

Our findings are important in that they describe the experience of one NICU's use of opioid infusions. Although our findings cannot be

generalized to all other NICUs, our experience may help to generate ideas for future research, both within and outside of our center.

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