Use of Intranasal Fentanyl in Palliative Care of Newborns and Infants

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Background

Neonatal deaths due to non-survivable congenital anomalies and perinatal conditions are a continued reality of newborn care. The need for a palliative approach can often be anticipated and prepared for when there is a prenatal diagnosis of a life-limiting fetal condition. Palliative care may also be appropriate when addressing the goals of care for seriously compromised neonates.
Fentanyl is a lipophilic, highly potent opioid that is readily absorbed through the transmucosal membranes and the blood-brain barrier. It is not irritating to the mucosa[1-3]. The T_{MAX} is 5[4]-15[5] minutes with therapeutic levels reported in as short as 2 minutes[6]. The onset of effect is within 5 minutes[7,8]. The bioavailability of fentanyl has been found to be 71[4]-89%[9].
There is a need to expand the pediatric and adult literature on intranasal use of the injectable preparation for the management of pain and dyspnea in newborns and infants at end-of-life.

Purpose

The purpose of this research was to evaluate the use, effectiveness, and safety of intranasal and buccal transmucosal fentanyl administration in newborns and infants 6 months of age or less.

Methods / Data Collection

A retrospective chart review with data collected from November 2006 through July 2010.

Results

A total of 58 charts were reviewed. Intranasal fentanyl was administered to 13 patients at end-of-life. This poster describes the two distinct patient groups in which fentanyl was administered – newborns and infants.

Information on Fentanyl Usage

	Newborn Group (n=8)	Infant Group (n=5)
Age at Death	15 minutes to 34 hrs and 35 minutes	28 days to 197 days
Starting Dose of Fentanyl Used (in mcg/kg/dose)	Range: 0.2-1.45 Mean: 0.86 Median: 0.75	Range: 0.8-3.8 * Mean: 1.7 Median: 1.0
Total Number of Fentanyl Doses Administered to Each Patient	Range: 1-17 Mean: 5.6 Median: 3.5	Range: 1-6 Mean: 3.6 Median: 4

** Note: Higher dose range used with patient who was receiving a 3 mcg/kg/hr intravenous fentanyl infusion. Only increased dose in one infant (from 0.8 to 1.7 to 2.5 mcg/kg/dose)*

NEWBORNS – INTRANASAL FENTANYL USE

ID #	Age at Death	Main Diagnosis	Gestational Age and Weight at Birth	Dose of Intranasal Fentanyl Ordered	Information on Intranasal Fentanyl Use	Documentation on Effectiveness of Intranasal Fentanyl	Other Medications Ordered and/or Used for Symptom Management
1	7 hrs, 45 minutes (min)	Anencephaly	38 weeks 2884 grams	Fentanyl 0.5 mcg/kg (= 1.4 mcg/dose) nasally or buccally q 15 min prn. Depending on effect may increase to 1-2 mcg/kg q 15 min prn.	Used 4 doses of 0.5 mcg/kg at: 3 hrs 45 min, 4 hrs, 15 min, 5 hrs 5 min, and 6 hrs 35 min of life. 4 doses used over a 3 hour period, with the last dose administered 70 min prior to death.	No charting about effectiveness of fentanyl.	Midazolam ordered, but not administered.
2	13 hrs, 9 min	Trisomy 18 with cardiac defect	41 weeks 1709 grams	Fentanyl 2.5 mcg (1.46 mcg/kg/dose) intranasal q 10 min prn for dyspnea. Increased to 5 mcg (2.9 mcg/kg/ dose) [but that dose not used].	Used 8 doses of 2.5 mcg. Doses given at 58 min, 1 hr 4 min, 2 hr 52 min, then 3 hr 40 min. At 9 hr and 5 min, a cluster of 4 doses given within 58 min. Increased dose to 5 mcg, but no further doses required. Last dose administered 3 hrs and 6 min prior to death.	Palliative Care Clinical Nurse Specialist note describing last 3 doses given: "Pt remained distressed – crying, extremely furrowed brow and another dose of fentanyl given at [time]. Continued to be restless and appeared distressed. So 2 more doses of fentanyl given. By [time – 19 min after last dose] pt was settled and was calm. Attempted by RN to help Mom breastfeed".	No other medications used for symptom management.
3	34 hrs, 35 min	Trisomy 13 with cardiac defect	36 weeks 2291 grams	Fentanyl 1.25 mcg (0.55 mcg/kg/dose) buccally q 15-20 min prn	9 doses used in total. Started using at 22 hrs and 10 min after birth. Used doses every 1-3 hours. Last dose was administered 60 min prior to death.	Nurse (15 min after 1st dose): "Fentanyl effective, infant calmer, HR 120, not tachypneic". Nurse (15 min after 2nd dose): "Infant had another apneic episode. Fentanyl given. Infant resting comfortably after". Palliative Care Physician note (after 3rd dose): "Had a couple cyanotic episodes with bradycardia + gasping breathing, which settled with fentanyl". Nurse (at time of 4th dose): "Cyanotic and gasping. Fentanyl given. Color improved. Respirations now rapid in 50's.Very shallow".	Midazolam was ordered to be given if fentanyl was not effective within 5 min. However, no midazolam was administered.
4	21 hrs, 23 min	Potter's Sequence	35 weeks 3154 grams	Fentanyl 2.5 mcg (0.8 mcg/kg/dose) nasally q 5 min prn for dyspnea.	17 doses, given at 8 min +13 min. Then 5 doses given every 90-120 min. Then a gap for 5 hrs, followed by 3 doses in a 25 min timeframe, a gap of 110 min and ten another cluster of 3 doses in 50 min. 40 min later a dose given and another 27 min after that. Last dose given 33 min prior to death.	Palliative Care Physician note: 'Baby having episodes of laboured breathing, effectively helped with nasal fentanyl 2.5 mcg".	No other medications used for symptom management.
5	9 hrs, 21 min	Intrauterine growth retardation, Premature	30 weeks 420 grams	Fentanyl 0.1 mcg (0.2 mcg/kg/dose) given intranasally q 15 min prn.	Used 3 doses total. Doses given at 2 hrs 11 min, 3 hrs 35 min, and 7 hrs 11 min. Last dose was administered 2 hrs and 10 min prior to death.	Palliative Care Physician note after 2 doses had been administered: "Both doses tolerated well without sequelae and seemed to alleviate symptoms".	Sucrose ordered, but no charting indicating number of times it may have been administered.
6	15 min	Giant ruptured oomphalocele	28 weeks 819 grams	Fentanyl 1mcg (1.2 mcg/kg/dose) q 5 min prn.	One dose 5 min after birth. Time of second dose not charted. Doses used for restlessness. Timing of last dose is unknown.	Palliative Care Physician note: "2 doses of fentanyl used for restlessness. Baby seemed comfortable at time of death".	No other medications used for symptom management.
7	1 hr, 20 min	Skeletal dysplasia	38 weeks 3422 grams	Fentanyl 2.5 mcg (0.7 mcg/kg/dose) intranasal prn.	One dose administered at 15 min after birth. This dose was administered 65 min prior to death.	Nurse charted 5 min after fentanyl given: "Colour pale. Appears comfortable, no distress at present. Occasional vocalizations, but RR slow, respirations shallow, HR approx 60/min". Palliative Care Physician note 20 note min after fentanyl given: "Comfortable. Minimal respiratory effort".	No other medications used for symptom management.
8	43 min	Polycystic kidney disease	35 weeks 3338 grams	Fentanyl 5 mcg (1.5 mcg/kg/dose) intranasal q 5 min prn.	One dose of fentanyl used 15 after birth at request of parents. This dose was administered 28 min prior to death.	Palliative care physician documentation: "No change in gasping rate, tone or colour after dose. No clinical effect noted. Parents seemed relieved that it was used."	No other medications used for symptom management.

INFANTS – INTRANASAL FENTANYL USE

ID #	Age at Death	Main Diagnosis	Brief Description of Respiratory Support	Dose of Intranasal Fentanyl Ordered	Information on Intranasal Fentanyl Use	Documentation on Effectiveness of Intranasal Fentanyl	Other Medications Used for Symptom Management
9	43 days	Multiple brain anomalies, likely mitochondrial disorder	PPV and NCPAP day 1 and 2. Oxygen via nasal prongs prn after that.	Intranasal fentanyl 5 mcg (1 mcg/kg/dose) every 15 min prn for distress	Used fentanyl of 33rd day of life for respiratory distress. Order discontinued on day 35 of life. The last dose given 10 days before death.	Nurse charted 10 min after administration: "Pt more settled now after fentanyl. Respiration are back to very shallow and regular as they had been."	No other medications used for symptom management.
10	28 days	Hypoxic-ischemic encephalopathy	Intubated and ventilated until day 10, then NCPAP until it was discontinued. Pt lived 2 hr 26 min after discontinuation of support	Fentanyl 2 mcg (1 mcg/kg/dose) nasally q 15 min prn for severe distress.	4 doses of fentanyl used in the 65 min after NCPAP discontinued. First dose was given at the time NCPAP stopped. The last dose given 81 min prior to death.	No charting about effectiveness of fentanyl.	Midazolam 0.2 mg q 15 min intranasally prn. Given 4 times in conjunction with intranasal fentanyl. Morphine – given 3 doses of 0.2 mg q 6 hourly prior to extubation. Glycopyrrolate 20 mcg via NG q 8 hrs.
11	44 days	Extremely premature, Necrotizing enterocolitis	Intubated and ventilated until it was discontinued. Pt lived 48 min after discontinuation of support.	Fentanyl 2 mcg (1 mcg/kg/dose) nasally q 15 min for severe distress	Intravenous site (which had been running fentanyl at 3 mcg/kg/hr) lost just prior to planned discontinuation of ventilatory support. 2 doses of fentanyl given prior to extubation and 2 doses administered at 3 min and 26 min after the extubation. The last dose was given 22 min prior to death.	NICU attending: "Extubated…some gasps, cyanotic. Looks settled". Nursing note after 2 doses: "Gave intranasal dosage of fentanyl and midazolam. Infant settled and appears well sedated and comfortable"	IJ line had been running a morphine infusion for over a month. Switched to fentanyl infusion 2 days prior to extubation, which was running at 3 mcg/kg/hr until just prior to extubation. Given one dose of intranasal midazolam 0.3 mg prior to extubation.
12	35 days	Hypoxic-ischemic Encephalopathy, Chromosome translocation	Intubated and ventilated until it was discontinued. Pt lived 25 min after discontinuation of support.	Fentanyl 5 mcg (3.8 mcg/kg/dose) intranasal q 5 min prn.	No intravenous line available. 3 doses of fentanyl used post-extubation within a 20 min period. The last dose was given 5 min prior to death.	No charting about effectiveness of fentanyl.	One dose of each of the following prior to extubation: Chloral Hydrate 110 mg via NG -2 hrs and 10 min prior), Morphine (0.1 mg/kg/dose) via NG – 1 hr and 3 min prior to extubation, Nozinan (0.1 mg/kg/dose) sublingual - 20 min prior to extubation, Midazolam 0.1 mg/kg/dose intranasal - 2 min prior to extubation. Post-extubation received 2 doses of Midazolam 0.2 mg/kg/dose intranasal (5 min after extubation and then 10 min after that).
13	197 days	Spinal muscular atrophy Type 1	On BiPap for the last month of life. Used BiPap most of the day (off 1-4 hours per day). Removed for last few min of life.	Fentanyl 5 mcg (0.8 mcg /kg /dose) nasally q 10 min prn. Dose increased to 10 mcg (1.7 mcg/kg/ dose) and then to 15 mcg (2.5 mcg/kg/ dose).	Ten days prior to death had sudden episode of respiratory distress when 3 doses of 5 mcg given within 35 min. Then 1 dose of 10 mcg given 2 hrs and 35 min later. Given 3 morphine breakthrough doses as well and regular morphine increased. On day of death used 2 doses of 15 mcg 1 hr and 40 min apart. Last dose given 50 min prior to death.	Ten days prior to death: started to settle with third dose. Fourth dose seemed to settle the breathing, despite increased muscle use, congestion and increased secretions.	Nozinan 1 mg NJ q 30 min prn. Used 1-4 doses per day in last 2 weeks of life. Midazolam 1 mg intranasal - used once when respiratory distress occurred 10 days prior to death. Morphine regular and prn doses started day 177 of life and used until death. Morphine started at 0.5 mg q4h and the same dose as breakthrough q 1h prn. Increased to 1mg until 10 days prior to death, then increased to 1.5 mg. Increased to 2 mg a couple days later and then increased to 2.5 mg on the day of death.

Discussion / Conclusions

- Administration of intranasal fentanyl to newborns and infants at end-of-life is safe and effective in managing respiratory distress
- Intranasal fentanyl is useful in a variety of care settings (hospital and home) for the management of symptoms in newborns and infants at end-of-life
- Identified the need to address logistical issues, which include: development of a guideline for the availability of the medication; the use of an atomizer in nasal medication delivery; and supporting staff in this approach to managing symptoms in newborns and infants at end-of-life.

Acknowledgements

This research is financially supported by The Manitoba Institute of Child Health

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