ORAL SWITCH OF CONTINUOUS INTRAVENOUS MORPHINE IN VENTILATED VERY PREMATURE INFANTS: A RETROSPECTIVE STUDY ON EFFICACY, EFFICIENCY AND TOLERANCE

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Background

Continuous intravenous (IV) morphine is commonly used in ventilated neonates¹. Oral route is theoretically feasible but data on oral morphine in ventilated premature infants are lacking. Most data on oral morphine currently available address neonatal abstinence syndrome.

Objective

After implementing a protocol for oral switch of IV continuous morphine in ventilated neonates, we aimed at assessing the efficacy, efficiency and tolerance of this protocol

Methods

Design & Setting

Retrospective study in a single level III center's Neonatal Intensive Care Unit.

Patients

Ventilated premature infants hospitalized in the NICU in 2016 and 2017, receiving continuous IV morphine and switched to oral morphine. We excluded patients treated for withdrawal syndrome or palliative care.

Intervention – Local protocol

In ventilated neonates receiving continuous IV morphine, the attending physician could decide to switch this treatment to the oral route if she/he expected that mechanical ventilation would last at least 3 more days and if enteral feeding was well tolerated. The oral daily dose was the same as the IV daily dose, divided in 4 doses (q6h) through a gastric tube.

Outcome measures

Pain scores (ComfortNeo scale²) and morphine doses were analyzed over time using Friedman's test (a non-parametric test for repeated measures) in the 24 hours preceding and the 48 hours following the oral switch. Ventilation parameters, digestive disorders (interruption of enteral feeding), urine retention, hypotension, occurrence of withdrawal syndrome after stopping morphine and use other analgesics/sedatives were also collected.

Results

Among 44 infants who received oral morphine during the study period, 17 fulfilled inclusion criteria.

Their characteristics are summarized in the Table below.

All but one were continued on oral morphine after the switch. In 1 patient, IV morphine was resumed 42 hours after the oral switch because of high ComfortNeo scores (=15).

Demographic and clinical characteristics of patients, N=17

Sex ratio (male/female)	10/17
Median (IQR) gestational age at birth (weeks)	25.9 (24.6 – 26.9)
Median (IQR) Birth weight (g)	670 (620 – 750)
Small for gestational age, n (%)	6 (35%)
Cause for intubation, n (%)	
Respiratory distress syndrome	7 (41%)
Repeated desaturations and apnea	8 (47%)
Bradycardia	1 (6%)
Surgery	1 (6%)
Median (IQR) postnatal age at the time of oral switch (days)	30 (22-36)
Median (IQR) postconceptional age at the time of oral switch (weeks)	30.4 (27.9 – 31.4)
Median (IQR) weight at the time of oral switch (g)	1070 (890 – 1230)

Results (cont'd)

No significant change over time was observed for **ComfortNeo scores** (p=0.15) (**Fig. 1**).

Median (IQR) **morphine doses** were 13.5 (10-20) µg/kg/h in the IV period and significantly increased to 15 (10-25) µg/kg/h in the oral period (p=0.009) (**Fig. 2**).

Eleven patients received benzodiazepine during the IV morphine period and 12 during the oral morphine period.

No significant change over time was observed for mean airway pressures (p=0.13) with median [IQR] values of 12.4 [10.7-13] and 10.6 [9.1-12.5] cm H₂O for the periods before and after the oral switch, respectively.

No significant change over time was observed for FiO₂ (p=0.24).

No digestive or urinary adverse event was observed. After a median (IQR) duration of oral morphine treatment of 13 (4-20) days, 11 (65%) patients showed signs of withdrawal.

Figure 1

Figure 2

Discussion

First report of oral morphine use in ventilated very premature infants.

Oral bioavailability might be higher in preterm than in term infants³ (mild increase in doses as compared to IV route).

However, increased doses at oral switch might be more effective.

Small sample, no long term assessment, no PK data

Conclusion

Oral morphine is a feasible alternative to IV morphine in ventilated neonates in the NICU but deserves further studies.

References

1: Carbajal R et al. *Lancet Respir Med*. 2015 Oct;3(10):796-812

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3: Liu T et al. *J Clin Pharmacol*. 2016;56(8):1009-18.