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Intubation in the delivery room: Experience with nasal midazolam ☆

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ABSTRACT

Background: Neonates are often intubated in the delivery room (DR) without anesthesia because vascular access is impossible.
Aims: To assess neonatal comfort and adverse events after use of nasal midazolam (nMDZ) for intubation in the DR.
Study design: Prospective data collection over 6 months on the intubation of neonates with respiratory distress requiring tracheal instillation of surfactant.
Subjects: Twenty-seven neonates with median (Q25–75) gestational age and birthweight of, respectively, 29 (27–33) weeks and 1270 (817–1942) g received a 0.1 mg/kg dose of nMDZ, and intubation was performed at the onset of tonus resolution or apnea.
Outcome measures: Comfort was assessed with a scale of hetero-pain assessment and electrical skin conductance monitoring. Continuous pulse oximetry was recorded in the first postnatal hour, with oscillometric blood pressure measurement every 10 min.
Results: Seventy percent of the patients required a single dose, with intubation performed 4.8 (3–9) min after administration. Combined electro-clinical assessment found adequate comfort during the procedure in 68% of neonates. Mean blood pressure decreased from 39 (34–44) mm Hg before to 31 (25–33) mm Hg 1 h following nMDZ ($p = 0.011$).
Conclusion: nMDZ provided rapid and effective sedation to intubate neonates in the DR but potentially exposed them to hypotension, thus requiring close hemodynamic monitoring.

1. Introduction

Neonatal endotracheal intubation is a very painful procedure that is commonly performed in the delivery room (DR). Except for intubations occurring in emergency situations, such as resuscitation, relieving and preventing pain are a therapeutic priority. Indeed, intubation in vigorous infants can cause systemic and pulmonary hypertension, bradycardia, intracranial hypertension and hypoxia [1]. Multiple attempts have also been implicated in upper airway injuries involving the pharyngo-esophageal, laryngeal and tracheal regions [2,3]. Although this message has been widely disseminated to all concerned medical and nursing staff, the pain management of neonates intubated in the DR is still frequently inadequate [4]. A recent survey in our country indicated that sedatives or analgesics in DRs were used in only 21% of the centers [5].

Sevoflurane and nitrous oxide inhalation have been proposed as an alternative to intravenous anesthesia, but this technique requires specific material or skills rarely found in the DR [6,7]. In cases of difficult vascular access, drug administration via nasal mucosa may also be considered [1]. Since 2009, we have used nasal midazolam (nMDZ) to intubate neonates in the DR, particularly premature neonates requiring rescue surfactant treatment. We were prompted to adopt this protocol because anesthesia before intubation was rarely administered in this situation due to the difficulty of accessing peripheral veins and the time required to place an umbilical venous catheter in sterile conditions. Furthermore, nMDZ has pharmacokinetic features that make it compatible with use in cases of urgent intubation; i.e., rapid action and high bioavailability [8]. Previous studies have also demonstrated nMDZ efficacy in reducing procedural anxiety [9] and treating acute seizures or status epilepticus in children [10,11]. Yet concerns have been raised about the safety of midazolam in neonates, with reports of altered hemodynamics, including decreases in heart rate, blood pressure and cerebral blood flow velocities [12,13]. These effects were nevertheless inconstant [14], transient [15] or of variable clinical significance [12,16] following an intravenous bolus. The findings on safety, particularly regarding neurologic outcome, remain contradictory in cases of

Abbreviations: nMDZ, nasal midazolam; DR, delivery room; NICU, neonatal intensive care unit; GA, gestational age; CPAP, continuous positive airway pressure; RTC scale, reactivity, tonus and consciousness scale; FANS, faceless acute neonatal pain scale; MABP, mean arterial blood pressure.

☆ This work was carried out in the delivery room of Arnaud de Villeneuve Hospital, CHU Montpellier, F-34000 France.

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prolonged infusion [17,18], and safety has never been assessed after a single intranasal administration.

Our purpose was thus to document our experience with this sedative regimen, particularly regarding neonatal comfort and adverse events occurring after nMDZ administered to intubate neonates in the DR.

2. Methods

2.1. Patients

This prospective observational study was performed in the DR and the level 3 neonatal intensive care unit (NICU) of a university hospital. Data were collected over 6 months, from February to September 2010. In accordance with our protocol, neonates received nMDZ when they met the following conditions: (i) inborn preterm neonates spontaneously breathing at 5 min of life, sometimes after a brief period of manual ventilation; (ii) neonatal respiratory distress, defined by a Silverman–Anderson retraction score [19] >3 in less than 30 week gestational age (GA) neonates and >5 in 30–34 week GA neonates; (iii) surfactant requirement, defined by a fractional inspired oxygen (FiO_2) >0.3 for less than 30 week GA and >0.4 for 30–34 week GA neonates; and (iv) normal blood pressure, defined as mean blood pressure >10th percentile of the reference range for GA or birthweight in the presence of intrauterine growth retardation.

nMDZ was not considered for neonates requiring immediate intubation; i.e., for Apgar scores <4, meconium aspiration syndrome, or major malformation like congenital diaphragmatic hernia. The efficacy of nMDZ was not evaluated for births occurring at night (6:30 pm to 8:30 am) or on holidays.

2.2. Protocol

Immediate postdelivery care was provided under a radiant warmer; the Apgar timer was started and a pulse oximeter sensor (Masimo low noise optical probe Neo) was placed on the infant's right hand or wrist as soon as possible and was then connected to an oximeter (Radical 7, Masimo, Irvine, CA, USA). After suction of nasal and oropharyngeal secretions, intermittent positive-pressure ventilation was provided, if necessary. Then, +5 cmH_2O continuous positive airway pressure (CPAP) ventilation was delivered using a device with a t-piece that attaches to a mask and a flow-controlled pressure-limited delivery system (Neopuff, Fisher & Paykel Healthcare, Auckland, NZ). Initial FiO_2 was 21% and was then adapted to obtain preductal pulse oximetry (SpO_2) between 60% and 65% at 1 min, 65% and 70% at 2 min, 70% and 75% at 3 min , 75% and 80% at 4 min , 80% and 85% at 5 min, and 85% and 92% at 10 min.

When the clinician decided to treat the respiratory distress at least 5 min after birth, nMDZ was administered using a 1-mL syringe at a dose of 0.1 mg/kg (0.1 mL/kg). After 5 s, CPAP was again started and maintained until the observation of hypnosis, clear muscular relaxation, or apnea, requiring intratracheal intubation. A second, similar dose of nMDZ was authorized if the neonate became aroused at the introduction of the tube in the nostril or if a neonate with persistent respiratory distress and FiO_2 requirements was excessively awake 5 min after the first dose. Blood pressure was monitored before any additional nMDZ dose. After intubation and verification of the adequate placement of the endotracheal tube, 200 mg/kg of poractant alfa (Curosurf, Chiesi, Parma, Italy) was administered.

2.3. Monitoring and comfort assessment during intubation

Monitoring included continuous pulse oximetry-derived heart rate and oxygen saturation and oscillometric blood pressure measurement (IntelliVue, Philips Medical Systems, Eindhoven, the Netherlands) before nMDZ administration and then every 10 min during the first postnatal hour. Clinical scales, skin conductance monitoring, and data on intubation were collected by a single observer (JB), who was not involved in patient care.

2.3.1. Clinical scales

The newborns were videotaped for 3 min before intubation and throughout the procedure, with a light and a field of vision allowing the observation of the entire body. The sound was set at a level that made any potential moaning or screaming easily audible. The videotapes were anonymized and then viewed by two independent observers. Each observer was blinded to the data collected by the other. Two scales were completed.

The Reactivity, Tonus and Consciousness (RTC) scale is a practical tool developed by a highly specialized team for neonatal transport in the Parisian region (SAMU 92). Reactivity, tonus and consciousness are quantified to define the depth of sedation just before intubation. Values range from 0, corresponding to an infant without reaction, clearly hypotonic and asleep when his head is positioned for intubation, to 8 in a patient with spontaneous movements, hypertonia, and full alertness in the same conditions [http://pediadol.org/IMG/pdf/Actes2006_137.pdf].

The Faceless Acute Neonatal pain Scale (FANS) was constructed and validated by our team [20] to assess pain in situations where observation of facial expression is not easy, which is precisely the case during intubation. This instrument evaluates both behavioral items, like body movements and vocal expression, and physiological items, like variation in heart rate, bradycardia or desaturation (Table 1). To increase the specificity of this scale, behavioral elements are given particular weighting, as they are strongly associated with acute pain in the preterm baby.

2.3.2. Skin conductance

Electrical skin conductance monitoring was performed via a Pain Monitor (Medstorm Innovations, Oslo, Norway). The electrodes were positioned as follows: measurement and counter on either side of the ankle, and reference on the sole of the foot. The equipment used an alternating current of 50 Hz and an applied voltage of 240 VAC (highest density 36 μA). The software automatically calculates the fluctuations in skin conductance activity and the frequency of the peaks reflecting the magnitude of the nociceptive stimulation [21]. The monitor was connected to a personal computer using an RS-232 serial communication port. A data sampling rate of 15 s, with a monitor refresh rate of 1 s, was selected, following the manufacturer's recommendations.

2.4. Outcomes

The main outcome was neonatal comfort during the procedure. To this end, we used clinical scales and skin conductance as follows:

- RTC score during intubation;
- FANS score before and during intubation;
- Electrical skin conductance data, from 2 min before nMDZ instillation to 2 min after intubation;

Table 1
Faceless Acute Neonatal pain Scale (FANS). Adapted with permission.

Heart rate variation	0: <10% 1: >10% 2: >50%
Acute discomfort	1: Bradycardia (FC <100 bpm) or desaturation SpO_2 <85%
Limb movements	0: Calm, slight 1: Mild intermittent with return to calm 2: Moderate 3: Marked, continuous 4: Global hypotonia
Vocal expression	0: Absent 1: Brief moaning, anxious 2: Intermittent screaming 3: Constant screaming