Drugs for Neonatal Intubation – Full Clinical Guideline

Reference no.: NIC RC 09/Dec 21/v004

1. Introduction

Endotracheal intubation is a commonly required procedure on the neonatal unit and it should be performed expeditiously in as controlled environment as possible to reduce physiological disturbances and complications. There are two aspects that need to be taken care of during neonatal intubation: minimising physiological disturbances and alleviation of pain. The physiological disturbances during the process of intubation results in hypoxemia[1], bradycardia[2], intracranial hypertension[3-5], systemic[1] and pulmonary hypertension[6,7]. In addition to the physiological disturbances poorly performed direct laryngoscopy can cause trauma to face, eyes, tongue, gums, arytenoids and other glottic structures. Both physiological disturbances and injuries can be avoided and intubation conditions enhanced by the use of premedication drugs[10-15].

It is important that all providers of neonatal care take steps to alleviate pain as repeated painful experiences in preterm neonates have the potential for long-term deleterious consequences[16]. A consensus statement from the International Evidence-Based Group for neonatal pain concluded “tracheal intubation without the use of analgesia or sedation should be performed only for resuscitation in the delivery room or for life threatening situations associated with the unavailability of intravenous access”[17].

The aim for the use of premedication for neonatal intubation is to achieve excellent intubation conditions characterised by good jaw relaxation, open and immobile vocal cords and suppression of pharyngeal and laryngeal reflexes assessed by the absence of coughing reflex[18].

Audit Points

1. How often do we use the policy when it is indicated?

2. What is the effect on physiological stability following drugs for intubation?

3. How often do the side effects of the drugs occur?

2. Aim and Purpose

Aim to provide intubation in a safe and controlled clinical environment using best evidence.

3. Definitions, Keywords

Intubation – inserting an endotracheal tube for ventilation

Intubation drugs – drugs used to facilitate safe intubation

4. Main Guideline

4.1 INCLUSION CRITERIA

4.1.1 Neonates receiving care on the neonatal unit:

All term and preterm neonates requiring elective intubation on the neonatal unit should receive pre intubation medication. The only exception being emergency life threatening conditions where the intubation is time-critical or the delay in intubation to obtain intravenous access, and prepare pre intubation medication could be fatal.

4.1.2 Preterm neonates

The use of pre-intubation medications in very small babies has not been well studied and available evidence is limited. However there is a theoretical benefit that use of pre-intubation drugs decreases the risk of raised intracranial pressure and hence IVH in extreme preterm infants and the limited evidence available on pre-intubation medication does not suggest an increase in any complications in this gestation group.

4.1.3 Intubation outside neonatal unit - on delivery suite/postnatal ward:

Intubations on delivery suite and postnatal ward are usually emergency intubations (not elective) and hence the procedure is time critical. It is also performed in difficult circumstances without intravenous access and delay in intubation could prove fatal. Hence use of pre-intubation medication in these situations would usually be inappropriate.

4.2 EXCLUSION CRITERIA

Airway management is always the first priority in managing a neonate with cardiorespiratory compromise.

Delaying intubation in order to give intubation drugs (such as whilst obtaining IV access) in a patient whose airway and breathing are not adequately controlled is not appropriate.

Exclusions, therefore, include but are not limited to:

1) Intubation on labour ward / theatres / postnatal wards.
2) Poorly perfused, apnoeic infants who do not respond to mask ventilation.
3) At delivery of infants with diaphragmatic hernia, where muscle relaxants are given once the airway is secured.
4) Difficult airways when caution should be exercised and consideration given to the loss of spontaneous respiratory drive once pre-intubation medications are given.

4.3 PREPARATION

Adequate preparation is the key to successful and minimally traumatic intubation. This should all take place and allow intubation to be commenced within 5 minutes.

4.3.1 Personnel

Senior personnel available should be present to perform or supervise intubation i.e. Registrar, Experienced ANNP or Consultant. If the personnel immediately present are not confident in intubation, experienced support should be summoned promptly PRIOR to any premedication drugs being given. It is crucial that nursing support is available throughout this procedure.

4.3.2 Patient

Prior to starting, it is essential to ensure the baby is adequately perfused and oxygenated. Pay careful attention to thermoregulation as preterm babies can get cold very quickly during the procedure. Following administration of intubation drugs it may be more difficult to maintain the airway and other manoeuvres, such as a two-person jaw thrust, may be necessary.

4.3.3 Drugs

The aim of pre-intubation medication is to decrease the physiological disturbances associated with intubation, and achieve optimal intubation conditions to decrease the duration and number of attempts needed for successful intubation.

Three groups of medications recommended to be used together for neonatal intubations include:

- Analgesic/sedative to control pain and discomfort
- Muscle relaxant to improve intubation conditions
- Vagolytic to prevent reflex bradycardia

There is limited evidence in neonates regarding the optimal choice of drugs in each of these categories. The combination listed here is based on best available evidence.

Table 1: Premedication for neonatal intubation

Medication group	**Action**	**Advantages**	**Complications**
Analgesic Fentanyl	Decrease pain and discomfort	Rapid onset of action Short duration of action	Chest wall rigidity, bradycardia, respiratory depression
Muscle relaxant Rocuronium	Achieves immobile neonate and vocal cords	Rapid onset of action Short duration of action	Can be reversed Less side effects as compared to

			depolarising muscle relaxants
Vagolytic Atropine	Prevents reflex bradycardia	Decreases oral and bronchial secretions Prevents/reverts reflex bradycardia	Urinary retention, GI dysmotility, tachycardia and cardiac arrhythmias.

4.3.1 Fentanyl

This is a potent, synthetic opioid analgesic with a rapid onset and short duration of action. The onset is almost immediate after intravenous administration, peak effect is seen at 5 – 15 minutes and the duration of analgesic effect is 30 – 60 minutes. It is important that fentanyl is given slowly over 30sec - 1min. There are case reports suggesting that a rapid bolus of fentanyl results in chest wall rigidity, making neopuff / bag mask ventilation extremely difficult. This can be prevented by very slow bolus over 30sec- 1min, or overcome by immediate administration of muscle relaxant.

4.3.2 Rocuronium

This is a non-depolarising muscle relaxant, which blocks nerve impulses to the muscles, resulting in paralysis. It is preferred over other depolarising muscle relaxants for its low side effect profile. The muscle relaxant, in this case Rocuronium should always be given after sedation has been achieved. Rocuronium starts working in about 1 minute (range 14 - 178 seconds), and its action lasts for about 16 minutes (range 1 – 60 minutes)[19]. If there is inadequate muscle relaxation after 5 minutes of administration, a repeat dose can be given.

If in an exceptional situation (such as inability to intubate), it is necessary for the paralysis to be reversed to allow the neonate to re-establish spontaneous breathing. Sugammadex, a Rocuronium antagonist, can be used (16mg/kg)[20]. The use of Sugammadex in neonates is unlicensed. It is the first selective relaxant-binding agent (SRBA). After giving Sugammadex (which would be an exceptional circumstance only), if muscle relaxant medication is required, Rocuronium may not be effective in baby for up to 24 hours and alternative muscle relaxant like Atracurium should be used.

4.3.3 Atropine

It is important that Atropine is always prescribed on the drug chart. This should be used in case of persistent reflex bradycardia with a sudden drop in heart rate. The saturations initially are maintained. Heart rate may drop with hypoxia as well. A drop in heart rate during intubation attempt should prompt a brief pause in the attempt and going back to mask ventilation. It is not necessary to routinely administer this drug. The reflex bradycardia can be avoided by ensuring that intubation is attempted when the baby is well sedated.

The pre-intubation medications should be prescribed on baby's prescription chart on the intubation drugs section for the baby's working weight.

4.4 Sedation post-intubation

Sedation should not be routinely used post-intubation. If sedation is required the use of morphine (10-20 mcg/kg/hour) would be the first choice. If muscle-relaxants are needed an atracurium infusion should be used. If this is introduced immediately after intubation a bolus dose may not be required. If the effects of rocuronium are no longer active then this may be used as per the monograph.

5. References (including any links to NICE Guidance etc.)

1. Marshall TA, Deeder R, Pai S, Berkowitz GP, Austin TL. Physiologic changes associated with endotracheal intubation in preterm infants. Crit Care Med. 1984;12(6):501-503.

2. Kelly MA, Finer NN. Nasotracheal intubation in the neonate: Physiologic responses and effects of atropine and pancuronium. J Pediatr. 1984;105(2):303-309.

3. Friesen RH, Honda AT, Thieme RE. Changes in anterior fontanel pressure in preterm neonates during tracheal intubation. Anesth Analg. 1987;66(9):874-878.

4. Raju TN, Vidyasagar D, Torres C, Grundy D, Bennett EJ. Intracranial pressure during intubation and anesthesia in infants. J Pediatr. 1980;96(5):860-862.

5. Marshall TA. Suctioning and cerebral blood flow. Pediatrics. 1984;73(5):737.

6. Hickey PR, Hansen DD, Wessel DL, Lang P, Jonas RA, Elixson EM. Blunting of stress responses in the pulmonary circulation of infants by fentanyl. Anesth Analg.1985;64(12):1137-1142.

7. Hickey PR, Hansen DD, Wessel DL, Lang P, Jonas RA. Pulmonary and systemic hemodynamic responses to fentanyl in infants. Anesth Analg. 1985;64(5):483-486.

10. Roberts KD, Leone TA, Edwards WH, Rich WD, Finer NN. Premedication for nonemergent neonatal intubations: A randomized, controlled trial comparing atropine and fentanyl to atropine, fentanyl, and mivacurium. Pediatrics. 2006;118(4):1583-1591.

11. Lemyre B, Cheng R, Gaboury I. Atropine, fentanyl and succinylcholine for non-urgent intubations in newborns. Arch Dis Child Fetal Neonatal Ed. 2009;94(6):F439-42.

12. Dempsey EM, Al Hazzani F, Faucher D, Barrington KJ. Facilitation of neonatal endotracheal intubation with mivacurium and fentanyl in the neonatal intensive care unit. Arch Dis Child Fetal Neonatal Ed. 2006;91(4):F279-82.

13. Pereira e Silva Y, Gomez RS, Marcatto Jde O, Maximo TA, Barbosa RF, Simoes e Silva AC. Morphine versus remifentanil for intubating preterm neonates. Arch Dis Child Fetal Neonatal Ed. 2007;92(4):F293-4.

14. Ghanta S, Abdel-Latif ME, Lui K, Ravindranathan H, Awad J, Oei J. Propofol compared with the morphine, atropine, and suxamethonium regimen as induction agents for neonatal endotracheal intubation: A randomized, controlled trial. Pediatrics. 2007;119(6):e1248-55.

15. Carbajal R, Eble B, Anand KJ. Premedication for tracheal intubation in neonates: Confusion or controversy? Semin Perinatol. 2007;31(5):309-317.

16. American Academy of Pediatrics, Committee on Fetus and Newborn, Canadian Paediatric Society, Fetus and Newborn Committee. Prevention and management of pain in the neonate. an update. Adv Neonatal Care. 2007;7(3):151-160.

17. Anand KJ, International Evidence-Based Group for Neonatal Pain. Consensus statement for the prevention and management of pain in the newborn. Arch Pediatr Adolesc Med. 2001;155(2):173-180.

18. Kumar P, Denson SE, Mancuso TJ, Committee on Fetus and Newborn, Section on

Anesthesiology and Pain Medicine. Premedication for nonemergency endotracheal

intubation in the neonate. Pediatrics. 2010;125(3):608-615.

19. Feltman DM, Weiss MG, Nicoski P, Sinacore J. Rocuronium for nonemergent intubation of term and preterm infants. J Perinatol. 2011;31(1):38-43.

20. BNF for Children. 2016 2017. BMJ Group, London.

6. Documentation Controls

Development of Guideline:	Dr A Wynn-Davies
Consultation with:	Neonatal Team
Approved By:	*Paediatric Business Unit Guidelines Group, Women and Children's Division – 21st December 2021*
Review Date:	December 2024
Key Contact:	Dr A Wynn-Davies

NHS
University Hospitals of Derby and Burton
NHS Foundation Trust

NICU INTUBATION CHART

Please affix Patient Label Here Patient Name _____ Date of Birth _____ NHS/ Hospital number _____	Date	**DRUG ALLERGY or ADVERSE EFFECT** If none known tick box ☐	
		Medication/Other	Nature of reaction / Source
	Working Weight (kg)		
		Signature (prescriber/pharmacist to complete)	Date

Drug	Instructions	Route	Prescriber Signature	Pharmacist Screen	Date & Time Required Signature	Date & Time Given	1st Nurse Signature	2nd Nurse signature
Fentanyl **(2 micrograms/kg)** =..... micrograms =..... mL (0.2mL/kg) of 10micrograms/1mL DILUTED SOLTN	Dilute 1mL of 50micrograms/mL with 4mL of glucose 5% to give a solution of **10 micrograms in 1mL**	Slow IV over 30 seconds			1st Dose Repeat Dose Repeat Dose			
Rocuronium **(600 micrograms/kg)** =..... micrograms =..... mL (0.6mL/kg) of DILUTED SOLTN	Dilute 1mL (10mg) of 10mg in 1mL solution to 10mL with glucose 5% to give **100 micrograms in 0.1mL**	Slow IV Bolus			1st Dose Repeat Dose Repeat Dose			
In the event of a bradycardia ensure adequate ventilation and give:								
Atropine **(20 micrograms/kg)** =..... micrograms =..... mL of	Dilute 600 micrograms (1mL) to 10mL with sodium chloride 0.9% to give **60 micrograms in 1 mL**	Slow IV Bolus						
In the event of failure to intubate-ventilate give: **Emergency reversal of Rocuronium** *(NOTE: if Sugammadex is given then Atracurium **MUST** be used for any subsequent intubations).*								
Sugammadex **(16mg/kg)** =..... mg =..... mL of DILUTED SOLTN	Dilute 100mg (1mL) to 10mL with sodium chloride 0.9% to give **10 mg in 1 mL**	Slow IV Bolus						

NHS
University Hospitals of Derby and Burton
NHS Foundation Trust

NICU INTUBATION CHART

INTUBATION DRUG DOSING GUIDE

Weight of Infant	0.5kg	1kg	1.5kg	2kg	2.5kg	3kg	3.5kg	4kg	4.5kg	5kg
FENTANYL										
Dose	1 microgram	2 micrograms	3 micrograms	4 micrograms	5 micrograms	6 micrograms	7 micrograms	8 micrograms	9 micrograms	10 micrograms
Amount of 10 micrograms per 1mL *diluted solution*	0.1 mL	0.2 mL	0.3 mL	0.4 mL	0.5 mL	0.6 mL	0.7 mL	0.8 mL	0.9 mL	1 mL
ROCURONIUM										
Dose	300 micrograms	600 micrograms	900 micrograms	1200 micrograms	1500 micrograms	1800 micrograms	2100 micrograms	2400 micrograms	2700 micrograms	3000 micrograms
Amount of 100 micrograms per 0. 1mL *diluted solution*	0.3 mL	0.6 mL	0.9 mL	1.2 mL	1.5 mL	1.8 mL	2.1 mL	2.4 mL	2.7 mL	3 mL
ATROPINE										
Dose	10 micrograms	20 micrograms	30 micrograms	40 micrograms	50 micrograms	60 micrograms	70 micrograms	80 micrograms	90 micrograms	100 micrograms
Amount of 60 micrograms per 1mL *diluted solution*	0.17 mL	0.33 mL	0.5mL	0.67 mL	0.83 mL	1 mL	1.17mL	1.33mL	1.5mL	1.67 mL
SUGAMMADEX										
Dose	8 mg	16 mg	24 mg	32 mg	40 mg	48 mg	56 mg	64 mg	72 mg	80 mg
Amount of 10 mg per 1mL *diluted solution*	0.8 mL	1.6 mL	2.4 mL	3.2 mL	4 mL	4.8 mL	5.6 mL	6.4 mL	7.2 mL	8 mL