Yorkshire & Humber Pan-Network Neonatal Clinical Guideline

Title:	**Pre-medications for Non-Emergency Neonatal Intubation**
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This clinical guideline has been developed to ensure appropriate evidence based standards of care throughout the Yorkshire & Humber Neonatal Operational Delivery Network. The appropriate use and interpretation of this guideline in providing clinical care remains the responsibility of the individual clinician. If there is any doubt discuss with a senior colleague.

A. Guideline summary

1. Aims

To provide evidence based recommendations for pre-medication prior to non-emergency intubation in neonates, in order to reduce medication errors and adverse events.

2. Best Practice Recommendations

To use fentanyl + atracurium +/- atropine for pre-medication for intubation of neonates.

3. Areas Outside Remit

This guideline is meant to be for the pre-medication selection and administration only. **It is not a teaching package for intubation.**

SECTION 1: Recommendation

We recommend the use of fentanyl 3micrograms/kg + atracurium 500micrograms/kg +/- atropine 10micrograms/kg for pre-medication for intubation of a neonate.
This combination provides effective analgesia, mild sedation and muscle relaxation to create good conditions for intubation[4].
We advise that all units using these drugs have naloxone available on the unit for the reversal of fentanyl effects if required[4]. We also advise that all units are aware of how to source neostigmine should it be needed for reversal of atracurium action.
We recognise that there may be situations in which propofol could be used as an alternative[5]. Please see Appendix 1.

FENTANYL + ATRACURIUM +/- ATROPINE FLOW CHART

Complete the pre-intubation section of the checklist.
ENSURE GOOD CONTROL OF AIRWAY IS MAINTAINED THROUGHOUT

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Give fentanyl 3 micrograms/kg **timed over three minutes** to avoid chest wall rigidity, followed by a slow IV flush of 2ml 0.9% sodium chloride also.
Then give atracurium 500 micrograms/kg over 1 minute followed by a slow IV flush of 2ml 0.9% sodium chloride.

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Pre-ventilate to target saturations for gestation. Attempt intubation. Do not spend longer than 30 seconds on each attempt. If unsuccessful re-ventilate to target saturations then re-attempt.

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If ventilation is difficult after administration of the pre-medications it may be due to chest wall rigidity. Ensure atracurium has been given and try increasing pressures slightly. If there is still difficulty then naloxone (100micrograms/kg) should be used for reversal of fentanyl effects.
If there is prolonged bradycardia **after adequate ventilation** then give 10micrograms/kg atropine.

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Complete post-intubation section of the checklist. Commence ongoing sedation +/- paralysis as needed.
Perform CXR and confirm position.
If ETT needs moving then document new position.

SECTION 2: 'READY RECKONER' chart for doses

WEIGHT	FENTANYL 3micrograms/kg	ATRACURIUM 500micrograms/kg	ATROPINE 10micrograms/kg	PROPOFOL 2mg/kg
0.5kg	1.5 micrograms	250 micrograms	5 micrograms	1mg
0.75kg	2.25 micrograms	375 micrograms	7.5 micrograms	1.5mg
1kg	3 micrograms	500 micrograms	10 micrograms	2mg
1.25kg	3.75 micrograms	625 micrograms	12.5 micrograms	2.5mg
1.5kg	4.5 micrograms	750 micrograms	15 micrograms	3mg
1.75kg	5.25 micrograms	875 micrograms	17.5 micrograms	3.5mg
2kg	6 micrograms	1 mg	20 micrograms	4mg
2.5kg	7.5 micrograms	1.25 mg	25 micrograms	5mg
3kg	9 micrograms	1.5 mg	30 micrograms	6mg
3.5kg	10.5 micrograms	1.75 mg	35 micrograms	7mg

SECTION 3: Drug Information

FENTANYL

Fentanyl is an opioid analgesic. It has a protective effect on intracranial pressure and blood pressure. It is reversible with naxolone.

Dose:
3 micrograms/kg (range 2-5 micrograms/kg)

Administration:
Fentanyl is a controlled drug.
It can be supplied and stocked on the unit as 10micrograms/ml.

If you have the 10 micrograms/ml strength draw up 0.3ml/kg to give a dose of 3micrograms/kg.

If you stock the 100micrograms in 2ml strength this needs to be diluted. Draw up 1ml and add to 4ml 0.9% sodium chloride. This gives a solution of 10 micrograms/ml. Draw up 0.3ml/kg of the diluted fentanyl to give 3micrograms/kg

Give final syringe a good mix prior to injection.

Give over **3 minutes** as a slow bolus to avoid chest wall rigidity. A timer/pump should be used to ensure accuracy with timing. Fentanyl may accumulate with repeat doses so consider reducing subsequent doses to 1 micrograms / kg (0.1 ml/kg of diluted solution)

Onset of action: 30-60 seconds

Duration of action: 30-60 minutes

Side effects: Apnoea, hypotension, CNS depression, chest wall rigidity (which can be treated with naloxone / muscle relaxants)

ATRACURIUM

Atracurium is a non-depolarising neuromuscular blocker. It should be given after fentanyl as it will paralyse but provide no sedation or analgesia to the baby. The muscle relaxation can be reversed with atropine followed by neostigmine.

Dose:
500 micrograms/kg

Administration:
Atracurium is supplied as 25 mg in 2.5ml.
It is kept in the fridge.

Draw up 0.5ml atracurium and add to 4.5ml of 0.9% sodium chloride.
This will give a solution containing 1mg/ml.
Then draw up 0.5ml/kg to give a dose of 500micrograms/kg.

Make syringe up immediately prior to use

Give over 1 minute to avoid significant cardiovascular side effects.

Onset of action: 2-4 minutes

Duration of action: 25-40 minutes

Side effects: Rarely bronchospasm and histamine release

NOTE: consider use of suxamethonium 2mg/kg if atracurium is not available.
Contraindications for suxamethonium should be checked and if using, atropine should be given routinely.

ATROPINE

Atropine is a vagolytic. It can counteract the bradycardic responses to the above drugs. It is not always necessary but can be drawn up for use if required.

Dose:
10micrograms/kg (20micrograms/kg if using with neostigmine to reverse atracurium)

Administration:
Atropine is supplied as 600 micrograms in 1ml. **Other strengths are used in some units - check before following this dilution advice.

Draw up 0.5ml of atropine and add to 2.5ml of 0.9% sodium chloride
This will give a solution containing 100 micrograms/ml.
Then draw up 0.1ml/kg to give a dose of 10micrograms/kg.

Onset of action: 30-60 seconds

Duration of action: 30-120 minutes

Side effects: tachycardia

NALOXONE

Naloxone is a short acting opioid antagonist used for overdose or unwanted side effects of opioids - in this setting, fentanyl.

Dose:
100micrograms/kg repeated at intervals of 1 minute up to a maximum total dose of 2mg.

Administration:
Naloxone is supplied as 400 micrograms in 1ml.

Draw up 0.5ml of naloxone and add to 0.5ml of 0.9% sodium chloride
This will give a solution containing 200 micrograms/ml.
Then draw up 0.5ml/kg to give a dose of 100micrograms/kg.

Onset of action: 60-120 seconds

Duration of action: 1-2 hours

Side effects: arrhythmia, hypertension, hypotension, rarely seizures

SECTION 4: Rationale

We recognise that there are many ways in which pre-medications can be combined and there is no single choice of combination to use[1,5]. There is a lack of robust trial data comparing pre-medication choices so the recommendation in this guideline has been made based on what little data there is, a wealth of experience and expert discussion and consensus.

We recognise that many of the references contained within this section are of low quality evidence. They add to the discussion rather than providing any guidance on choice via results of good randomised controlled trials.

Fentanyl is a short acting opioid with rapid onset of action. Although clinical trial and research data is lacking for all of the pre-medications for neonatal intubation, there is a wealth of experience of fentanyl use in the UK and worldwide[4]. Many studies include fentanyl in their protocols though few have done direct comparisons with other opioids[12].

The side effect of chest wall rigidity with fentanyl is a serious one, so we advise giving fentanyl slowly to avoid this[4,22]. We recommend giving fentanyl over three minutes, and to time this three minutes. A fentanyl dose of 3micrograms/kg has been chosen which lies within the recommended dose range[22], aiming to achieve good analgesia and some sedation, but to avoid side effects as much as possible.

We have not recommended morphine due to its much longer onset of action and longer duration of action[1,4,5,14].

Atracurium has been chosen, again due to the large amount of experience many units have with its use. There is limited evidence to assess its superiority over other muscle relaxants though it does feature in some study protocols[13]. It acts quickly and has few side effects, though bronchospasm is recognised[22]. Its duration of action is longer than some of the other muscle relaxants. We have chosen a dose of 500micrograms/kg, which is within the recommended dosing[22].

Pancuronium is the non-depolarising muscle relaxant which has been most studied in neonates but it has a longer onset and duration of action. Pancuronium's long action may make this helpful for longer term muscle relaxation in ventilated infants but the prolonged effect is not a helpful property as a muscle relaxant for intubation. Therefore we do not recommend it for a pre-medication for intubation.

In the past many units have used suxamethonium, a depolarising muscle relaxant. It has beneficial rapid onset and short duration of action. Unfortunately suxamethonium has a number of side effects, interactions and contraindications[1]. It also requires the concomitant use of atropine to counteract the frequently occurring bradycardia particularly with repeated doses[4,7,11]. Therefore we do not recommend its use as a pre-medication for intubation.

Atropine is also used to negate the vagal causes of bradycardia which can occur during intubation. There is discussion in the literature about how often bradycardia seen at intubation is hypoxia-induced rather than being caused by laryngeal stimulation[4]. The need for atropine as part of the pre-medication selection in neonates has not been well studied[4,5]. Whilst there is some low level evidence for its use[9], some authors are now disputing the need for atropine as part of the pre-medication combination[8,10]. Further discussion in the literature suggests that atropine is only required with repeated doses of suxamethonium when cardiac arrhythmia is a potential side effect[7,11].

Given that we have not recommended the use of suxamethonium, and our units have experience of not routinely using atropine with no untoward outcomes, we have agreed that there is not a need to give atropine routinely. As such, we have recommended that atropine be available should it be required. Some units may choose to have it ready drawn up and others may choose to draw it up only if required. We have recommended a standard dose of 10micrograms/kg[22].

Propofol has not been chosen as our first line recommendation for units across the ODN, though there has been considerable experience of its use in one of our NICUs. There are significant concerns in the literature and some evidence regarding its side effect profile, in particular the hypotension that can occur after administration[16,17,18,19,20,21]. There is one trial concluding superiority over morphine atropine and suxamethonium[15], But none over our specified combination of pre-medications[2,3]. NICE do recognise it as an option for pre-medication[5].

There are some studies hypothesising that the recognised side effect of hypotension is 'permissive'[16] as it seems to have little effect on cerebral saturations[18]. Some studies do not report issues with hypotension at all[15].

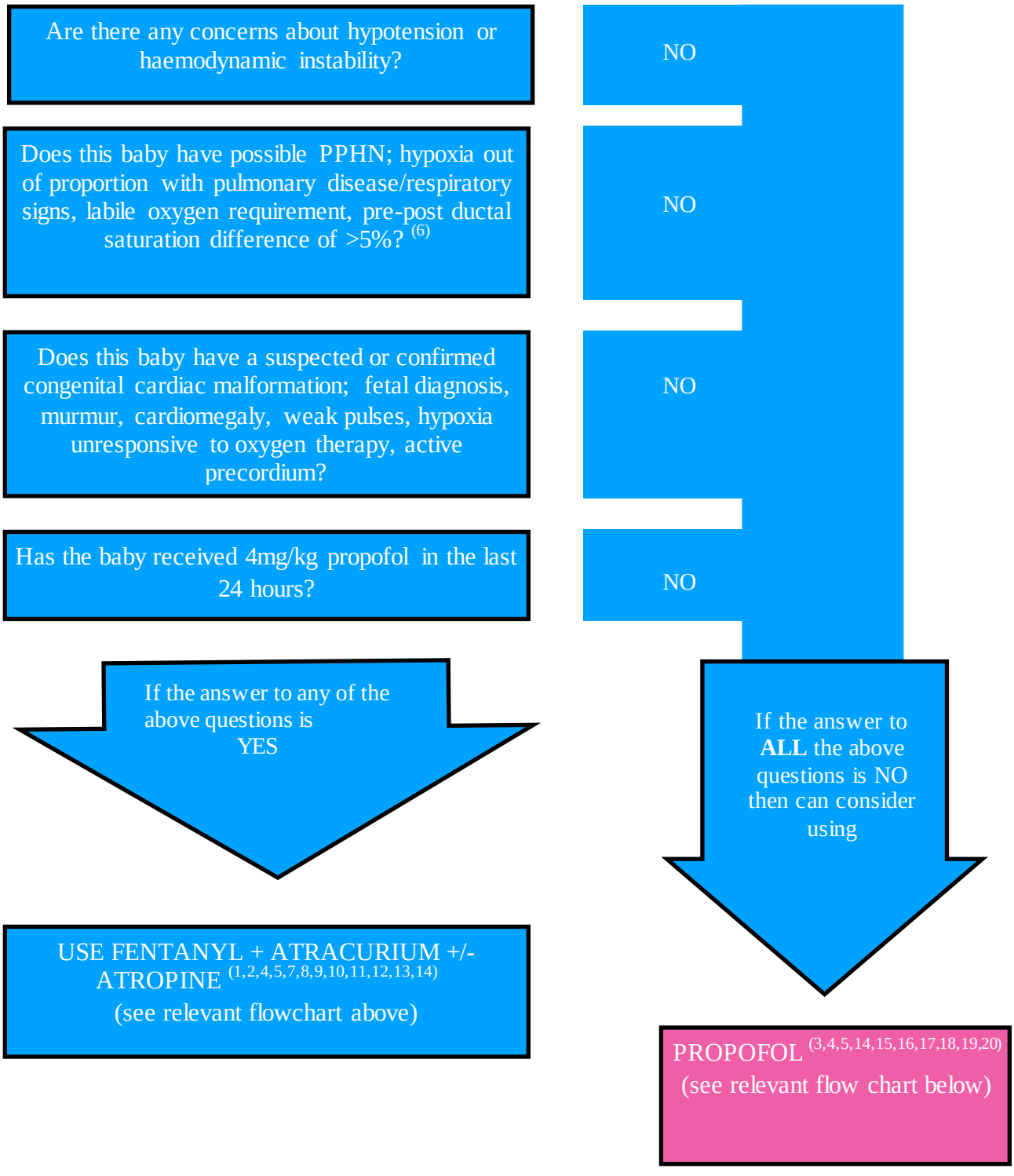
The major advantage with propofol is the speed at which the pre-medications are ready[3,]. It is a single agent regime and does not require complicated dilutions.

The dose for propofol has not been well established. Some studies advised/used 1-2mg/kg[16,18,19], some found doses up to 3.3mg/kg were needed on average[17], and others were unable to find a specific dose that gave the desired effects without significant side effects[20,21]. There is no recommended dose for neonates in the BNFc. In anaesthetic practise propofol is used by titrating to effect so each individual receives the minimum dose necessary to achieve sedation[24]. For completeness we have included the propofol pathway being used in Leeds as an appendix (see Appendix 1).

SECTION 5: APPENDICES

APPENDIX 1 - Using propofol as an alternative

Propofol can be used as an alternative pre-medication in units who have experience of its use but we are **not** recommending this for routine use. The following decision making tool should be used to establish whether a particular patient may be suitable for sedation with propofol.



DRUG INFORMATION

PROPOFOL [16,17,21,22]

Propofol acts as a hypnotic and muscle relaxant and can therefore be used as a single pre-intubation agent.

Dose:
2mg/kg plus further doses of 1mg/kg can be given as required to achieve sedation (up to 4mg/kg can be given in 24 hours).

Administration:
Propofol 0.5% is supplied as 100mg in 20ml.
It is kept in the IV cupboard.

It does not need dilution.
Draw up 0.4ml/kg of 0.5% (5mg/ml) propofol to give a dose of 2mg/kg.

Give as a slow bolus over 2 minutes followed by slow IV flush (2 ml of 0.9% sodium chloride) over a further 2 minutes to minimise the side effects. If adequate sedation is not achieved then given further dose after 2 minutes.

Onset of action: 30-60 seconds

Duration of action: 3-10 minutes

Side effects: hypotension, persistent hypoxaemia, bradycardia, chronic convulsion, localised muscle twitching (usually self-limiting) and pain at injection site. Muscle twitching is more frequently observed after rapid and / or repeated doses but these are self-limiting and not harmful.

PROPOFOL FLOW CHART

Complete the pre-intubation section of the checklist
ENSURE GOOD CONTROL OF AIRWAY IS MAINTAINED THROUGHOUT

Use propofol 0.5% 2mg/kg slow IV infusion over 1-2 minutes followed by slow IV flush of 2ml 0.9% sodium chloride.

Have 10ml/kg 0.9% sodium chloride drawn up in case of significant hypotension [21,22]

Pre-ventilate to target saturations for gestation. Attempt intubation. Do not spend longer than 30 seconds on each attempt. If unsuccessful re-ventilate to target saturations then re-attempt.

Check blood pressure every five minutes for 15 minutes then every 15 minutes for an hour. If low, assess perfusion and, if there are concerns, then give 10ml/kg 0.9% sodium chloride and re-assess.

Complete post-intubation section of the checklist. Commence ongoing sedation +/- paralysis as needed.
Perform CXR and confirm position.
If ET tube needs moving then document new position.

APPENDIX 2: Drug Calculator

See appendix 2 – standalone document.

APPENDIX 3: Additional Recommendations

1. The use of a 'ready reckoner' or drug calculator that can be printed for individual patients in preparation for potential intubation. For example, printed every week/month in line with weight gains and pinned to the incubator/cot/bedspace
2. Pre-made syringes could reduce the time taken to have pre-medications available. This may be something worth discussing with pharmacy.
3. Individual units should add an audit of intubation to their rolling audit programme to monitor complications/untoward events.
4. Individual units should feedback any such untoward events to the ODN via the clinical forum.

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