Policy Directive

Women and Babies: Pre-medication for intubation

Document No: RPAH_GL2014

Functional Sub-Group: Clinical Governance

Summary: Describes the drugs used for intubation

National Standard: Standard 1: Governance for safety and quality in Health service organisations
Standard 9: Recognising and responding to clinical deterioration in acute health care

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Approved by: General Manager
RPA Women and Babies Service Improvement Committee

Publication (Issue) Date: July 2016

Next Review Date: July 2019

Compliance with this Guideline is recommended
Replaces Existing Policy: Pre-medication for intubation and drugs for sedation/analgesia during ventilation

Previous Review Dates: 2000

Note: Sydney Local Health District (LHD) and South Western Sydney LHD were established on 1 July 2011, with the dissolution of the former Sydney South West Area Health Service (SSWAHS) in January 2011. The former SSWAHS was established on 1 January 2005 with the amalgamation of the former Central Sydney Area Health Service (CSAHS) and the former South Western Sydney Area Health Service (SWSAHS).

In the interim period between 1 January 2011 and the release of specific LHN policies (dated after 1 January 2011) and SLHD (dated after July 2011), the former SSWAHS, CSAHS and SWSAHS policies are applicable to the LHDs as follows:

Where there is a relevant SSWAHS policy, that policy will apply
Where there is no relevant SSWAHS policy, relevant CSAHS policies will apply to Sydney LHD; and relevant SWSAHS policies will apply to South Western Sydney LHD.
Women and Babies: Pre-medication for intubation

1. Introduction

The risks addressed by this policy:

| Potential complications of analgesics and sedatives used as premedication for intubation in term and preterm babies. |

The aims / expected outcome of this policy:

| To safely provide adequate pre-medication for semi-elective and elective intubation of neonates. |

2. Policy Statement

A policy statement should provide direction to all staff and clearly reflect the requirements of relevant legal / statutory regulations and / or service requirements.

3. Guidelines

3.1 Background

Intubation is a common procedure in newborn intensive care units. Intubation can cause traumatic injury to the airway and lead to cardiorespiratory instability during the procedure. The use of premedication reduces the adverse physiological responses of bradycardia, systemic hypertension, intracranial hypertension and hypoxia. The use of premedication decreases the pain and discomfort associated with the procedure. In 2010, the American Academy of Pediatrics (AAP) recommended premedications for all intubations in neonates, except in the emergent intubation during resuscitation.

3.1.1 Sedation / muscle relaxation and intubation?

Studies have unequivocally demonstrated that premedication of infants who require intubation with various forms of induction agents increases the speed of successful intubation and reduces the likelihood of the occurrence of associated adverse sequelae. In a study by Oei et al in preterm and term infants who were randomised to morphine, suxamethonium and atropine or no medication, the pre-medicated babies took fewer attempts (median 2 vs 1) and were significantly faster (median 60s vs 595 seconds). Bhutada et al compared thiopentone with no premedication in term babies and also showed a shorter intubation time.
3.1.2. What we do at RPA?

Fentanyl is the drug of choice for elective/semi-elective intubation in neonates with intravenous morphine as an alternative. A muscle relaxant should always be used with fentanyl.

The procedure

1. Prepare all the necessary equipment required for the procedure
2. Prescribe and prepare the intubation medications
3. Administer the medications in the following sequence. Fentanyl needs to be given slowly over 30-60s to avoid chest wall rigidity

4. Contra-indications to succinylcholine include significant hyperkalaemia, a family history of malignant hyperthermia and suspicion of muscular dystrophy
5. Naloxone needs to be available on the resuscitation trolley in case of chest wall rigidity.
6. If morphine is used as an alternative then the order of administration is morphine, atropine and then succinylcholine. It needs to be administered 1-5 minutes prior to intubation for good effect.
**Medication Dosages**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Effect</th>
<th>Dosage</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl</td>
<td>Analgesic</td>
<td>4 microgram/kg</td>
<td>IVI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Consider a reduced dose (2 micrograms/kg) if &lt; 34 weeks</td>
<td></td>
</tr>
<tr>
<td>Succinylcholine</td>
<td>Muscle Relaxant</td>
<td>2 mg/kg</td>
<td>IVI</td>
</tr>
<tr>
<td>Atropine</td>
<td>Vagolytic agent</td>
<td>10 microgram/kg</td>
<td>IVI</td>
</tr>
<tr>
<td>Morphine</td>
<td>Analgesic</td>
<td>200 microgram/kg</td>
<td>IVI</td>
</tr>
<tr>
<td>Naloxone</td>
<td>Opioid Antagonist</td>
<td>10 microgram/kg</td>
<td>IVI</td>
</tr>
</tbody>
</table>

### 3.1.3. Drugs for intubation in newborns. What are our options?

**Fentanyl and Remifentanil**

Fentanyl is a widely used opiate in newborns and children. It has a very rapid onset of action related to its lipophilic nature. A bolus IVI injection produces a rapid effect that diminishes after 30 minutes as the drug is redistributed in fat and muscle. Fentanyl clearance during the first few days of life is correlated with gestational age and birth weight; the more immature smaller babies having reduced plasma clearance due to immaturity of hepatic enzymes. 5,6 Fentanyl has not been studied as a single agent in intubation in neonates; however, a cohort study of 33 preterm and term infants intubated after atropine, fentanyl and a paralytic agent showed that fentanyl had no significant adverse events. 7 Adverse events reported with fentanyl include apnoea, hypotension, CNS depression and chest wall rigidity.8 Fahnenstich et al 8 observed chest wall rigidity in 8 and laryngospasm in 2 out of 189 term and preterm infants sedated with fentanyl. The risk of chest wall rigidity is reduced if given slowly. The rigidity can be reversed with muscle relaxants or naloxone. A randomised control trial comparing fentanyl to morphine as analgesia for ventilated newborns showed equal efficacy with fentanyl having fewer side effects. 10 In a randomised control trial comparing remifentanil to fentanyl, the time to successful intubation was not different between the groups; however, there was a non-statistically significant increase in chest wall rigidity in the remifentanil group.11 Remifentanil was as effective as a combination of morphine and midazolam for intubation in infants > 28 weeks with no difference in adverse events. 12 Pre-medication with remifentanil demonstrated good analgesic effect for intubation in premature infants; however the pharmacokinetics of remifentanil metabolism in early neonatal life has not been well evaluated. 13 The AAP recommends fentanyl as the preferred agent for analgesia during intubation. 14

**Morphine**

This is the most widely used and probably the best studied premedication sedative in Australia and the UK. Intravenous morphine has a mean onset of action at 5 minutes and a peak effect at 15 minutes. 15 The half life is inversely related to gestational age, being 6 and 12 hours in the very preterm infant. Full pain relief requires a blood level over 120ng/ml.15 Hartley et al showed this level was not achieved by 100micrograms/kg (mean level 99ng/ml) but was more reliably achieved by 200 micrograms/kg (mean level 180 ng/ml).15 The main advantage of Morphine is that it is the drug with which we have the most experience in newborn sedation/analgesia.

**Propofol**

Propofol is a lipid-soluble, hypnotic agent that has a very rapid onset of action and in which spontaneous respiration is maintained in most instances. Maintaining spontaneous respiration is advantageous in the neonate who is not successfully intubated because an airway is maintained.
randomised control trial demonstrated that propofol was superior over morphine, suxamethonium and atropine for the facilitation of elective neonatal intubation with fewer multiple attempts and better oxygenation during the procedure and recovery. A prospective observational study showed that in most babies a starting dose of 2mg/kg was insufficient to achieve adequate sedation (mean of 3.3mg/kg required) which was not related to gestational age or body weight. There was a statistically significant decrease in blood pressure after propofol administration compared with baseline. Welzing also described significant blood pressure instability in preterm infants administered propofol even at small doses. Propofol needs to be used in caution in preterm infants.

Ketamine

Ketamine is a widely used analgesic and anaesthetic agent in children and neonates. It is a NMDA (n-methyl D-aspartate) receptor antagonist but it also alters receptor function at dopaminergic, serotonergic and cholinergic sites. It has a relatively safe haemodynamic and respiratory profile. An observational pilot study using ketamine and atropine in the delivery room during intubation demonstrated reduced pain and less vagal bradycardia compared to controls. There has been some association with hallucinations, increased ICP and neuronal death in an immature brain after repeated high doses which have limited its use. Ketamine is a widely used analgesic and anaesthetic agent in children and neonates. It is a NMDA (n-methyl D-aspartate) receptor antagonist but it also alters receptor function at dopaminergic, serotonergic and cholinergic sites. It has a relatively safe haemodynamic and respiratory profile. An observational pilot study using ketamine and atropine in the delivery room during intubation demonstrated reduced pain and less vagal bradycardia compared to controls. There has been some association with hallucinations, increased ICP and neuronal death in an immature brain after repeated high doses which have limited its use. Ketamine is a widely used analgesic and anaesthetic agent in children and neonates. It is a NMDA (n-methyl D-aspartate) receptor antagonist but it also alters receptor function at dopaminergic, serotonergic and cholinergic sites. It has a relatively safe haemodynamic and respiratory profile. An observational pilot study using ketamine and atropine in the delivery room during intubation demonstrated reduced pain and less vagal bradycardia compared to controls. There has been some association with hallucinations, increased ICP and neuronal death in an immature brain after repeated high doses which have limited its use. Ketamine is a widely used analgesic and anaesthetic agent in children and neonates. It is a NMDA (n-methyl D-aspartate) receptor antagonist but it also alters receptor function at dopaminergic, serotonergic and cholinergic sites. It has a relatively safe haemodynamic and respiratory profile. An observational pilot study using ketamine and atropine in the delivery room during intubation demonstrated reduced pain and less vagal bradycardia compared to controls. There has been some association with hallucinations, increased ICP and neuronal death in an immature brain after repeated high doses which have limited its use.

Thiopentone

Thiopentone is a barbiturate with hypnotic and anticonvulsant effects but no analgesic effects. Bhutada et al showed that using thiopentone shortened the time to intubation compared with placebo; however had an increased heart rate and decreased blood pressure. Norman studied thiopentone in preterm babies and found it effective for semi-urgent intubation.

Midazolam

Midazolam is a useful sedative but has no analgesic effects. It has a rapid onset of action but in kinetic studies in term and preterm infants it has been shown that the half-life of midazolam given as a continuous infusion or by repetitive dosing can exceed 22 hours. Withdrawal, encephalopathy, hypotension, respiratory depression, agitation and myoclonus have all been described. In a randomised control trial (ceased early due to adverse events) in preterm infants who received midazolam and atropine for intubation, they have increased desaturations and nearly 30% required cardiopulmonary resuscitation compared to the control group. Midazolam should not be used in preterm infants.

Muscle relaxants

The ideal muscle relaxant for intubation has a rapid onset and short duration of action with minimal or no effect on heart rate and blood pressure. Succinylcholine, a depolarizing agent has an onset of action of 30 seconds and duration of action of 3-6 minutes which makes it ideal for intubation. The use of muscle relaxants during intubation minimizes the increase in intracranial pressure that occurs with awake intubation. This has been demonstrated with succinylcholine (a depolarizing agent) in preterm infants and pancuronium (non-depolarizing agent) in preterm and term infants. The use of succinylcholine with morphine and atropine in preterm babies results in less trauma, less bradycardia and faster intubation. Contra-indications to suxamethonium include significant hyperkalaemia, a family history of malignant hyperthermia and suspicion of muscular dystrophy. Pancuronium has a slower onset of action and longer duration therefore is not used for intubation.

4. Key Points

<table>
<thead>
<tr>
<th>Key Points</th>
<th>Level of evidence</th>
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</thead>
<tbody>
<tr>
<td>Sedation and muscle relaxation for intubation results in fewer attempts and is significantly faster</td>
<td>II</td>
</tr>
<tr>
<td>Fentanyl is the rapid acting analgesic of choice for elective intubation in neonates</td>
<td>II</td>
</tr>
</tbody>
</table>

Compliance with this Guideline is recommended
Chest wall rigidity is a rare complication of fentanyl. This can be avoided by using muscle relaxants and by a slow IVI infusion

Midazolam infusions in preterm infants are associated with adverse neurological outcomes

5. References


Revised by Dr Tracey Lutz (2016)