Premedication before intubation in UK neonatal units

Simon Whyte, Ginny Birrell, Jonathan Wyllie

Abstract

Aims—To establish the extent and type of premedication used before intubation in neonatal units in the United Kingdom.

Methods—A structured telephone survey was conducted of 241 eligible units. Units were subdivided into those that routinely intubated and ventilated babies (routine group) and those that transferred intubated and ventilated babies (transfer group).

Results—Of the units contacted, 239 (99%) participated. Only 88/239 (37%) gave any sedation before intubating on the unit and only 34/239 (14%) had a written policy covering this. Morphine was used most commonly (66%), with other opioids and benzodiazepines used less frequently. Of the 88 units using sedation, 19 (22%) also used paralysis. Suxamethonium was given by 10/19 (53%) but only half of these combined it with atropine. Drug doses varied by factors of up to 200, even for commonly used drugs.

Conclusion—Most UK neonatal units do not sedate babies before intubating, despite evidence of physiological and practical benefits. Only a minority have written guidelines, which prohibits auditing of practice.

Keywords: intubation; premedication; sedation

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Table 1 Numbers (%) of units with policies or regular practices for elective and emergency intubations/reintubations

<table>
<thead>
<tr>
<th>Routine</th>
<th>Transfer</th>
<th>Total</th>
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<tr>
<td>(n=190)</td>
<td>(n=49)</td>
<td>(n=239)</td>
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Written policy for elective intubation/reintubation 31 (16) 3 (6) 34 (14)
Also used for emergency intubation/reintubation 18 (9) 1 (2) 19 (8)
Regular practice for elective intubation/reintubation (no written policy) 43 (23) 7 (14) 50 (21)
Also used for emergency intubation/reintubation 15 (8) 3 (6) 18 (8)
Written policy only for emergency intubation/reintubation 3 (2) 1 (2) 1 (0.4)
Regular practice only for emergency intubation/reintubation 113 (59) 38 (78) 151 (65)
No sedation for any intubation/reintubation

Table 2 Sedatives used by UK neonatal units before intubation

<table>
<thead>
<tr>
<th><em>Routine</em> (%)</th>
<th><em>Transfer</em> (%)</th>
<th><em>Total</em> (%)</th>
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<tbody>
<tr>
<td><em>(n=77)</em></td>
<td><em>(n=11)</em></td>
<td><em>(n=88)</em></td>
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Morphine alone 29 (38) 8 (73) 37 (42)
Morphine + other† 20 (26) 1 (9) 21 (24)
Fentanyl alone 4 (5) 4 (4.5)
Fentanyl + other 4 (5) 4 (4.5)
Fentanyl: total 8 (10) 8 (9)
Diamorphine 11 (14) 1 (9) 12 (14)
Diazepam alone 4 (5) 4 (4.5)
Diazepam + opioid 6 (8) 6 (7)
Diazepam: total 10 (13) 10 (11.5)
Midazolam alone 4 (5) 4 (4.5)
Midazolam + opioid 2 (3) 2 (2)
Midazolam: total 6 (8) 6 (6.5)
Ketamine 1 (1) 1 (1)
Phenobarbitone 1 (9) 1 (1)

*Sum of percentages exceeds 100% because some units give opioids and benzodiazepines.
†See figure 1.
Results
All 245 units listed were contacted. Two declined to participate and three others had relocated their services. One further unit did not accept any premature deliveries. The sample therefore comprised 239 units, of whom 190 were in the routine group.

PROVISION OF SEDATION
Table 1 summarises the questionnaire data, illustrating that 63% of all units and 59% of the routine group gave no sedation before intubating on the unit. The overall average was increased by the transfer group, 78% of whom gave no sedation before intubating. There were 34/239 units (14%) with a formal written policy for sedating before elective intubation, with 31/190 (16%) in the routine group, and 3/49 (6%) in transferring units.

Overall, 8% (19/239) of units had a written policy that was applied during elective and emergency intubations on the neonatal unit. A further 8% (18/239) routinely gave sedation before all intubations but did not have a written policy.

Key messages
- There is good evidence of physiological and practical benefit when neonates are sedated before intubation, and no evidence that it is harmful.
- Only 37% of UK neonatal units routinely sedate babies before intubating them on the unit.
- Only 14% of units have formal guidelines for sedation before intubation, prohibiting audit of practice.

DRUGS USED
Eighty eight of the 239 units (37%) gave some form of sedation before intubation as detailed in table 2. Morphine was used most often (58/88; 66%). Around two thirds of these used it as the sole drug administered, but this was more representative of the transferring units, 73% of whom gave morphine in isolation, compared with 38% of units that routinely ventilated.ﻢ

Only one transferring unit co-administered morphine (11%), while a quarter of all routinely ventilating units gave an additional drug with morphine (fig 1).

In the 30/88 units not using morphine, 20 used an alternative opioid, with 12 giving diamorphine as the sole agent for sedation, and eight using fentanyl either alone (n=4) or in combination with suxamethonium (n=1), atracurium (n=1), and diazepam (n=2). Benzodiazepines were used for sedation before intubation by 16 units, all of whom routinely ventilated. Ten used diazepam (four alone, four with morphine, two with fentanyl) and six used midazolam (four alone, two with morphine).

One surgical unit used ketamine, in combination with suxamethonium and vecuronium. One transferring unit used phenobarbitone.

Muscle relaxants were used by 19/88 units (22%); all co-administered sedative drugs (table 3). Table 4 documents the substantial variation in prescribed doses between units.

Discussion
Neonates respond adversely to various neonatal intensive care practices11 12 and several investigators have studied the physiological responses of neonates to awake intubation,2 5 9 9 reporting significant rises in systemic arterial blood pressure and intracranial pressure, as well as significant falls in heart rate and transcutaneous oxygen tensions or saturations. Concern has also been raised about the contribution of raised intracranial pressure1 5–17 to the aetiology of intraventricular haemorrhage.

Premedication can improve or abolish these potentially deleterious responses. Bradycardia can be abolished by the use of atropine1 or glycopyrrolate, while rises in intracranial pressure have been attenuated by using muscle relaxants alone2 5 9 and combined with intra-
venous anaesthetics. Friesen et al reported a mean increase in anterior fontanellar pressure of 197% in one group of premature neonates who were intubated awake compared with 25% in a matched second group, who received premedication before intubation. The use of suxamethonium can shorten the procedure of intubating neonates, thus reducing the incidence and duration of the hypoxaemia that commonly occurs.

This study is an accurate representation of the current state of UK practice on premedication for intubation. The questionnaire was quick and easy to administer, with unambiguous questions, each addressing a single point, and requiring simply a yes or no response in most cases. Only two people made calls, thus achieving a high level of consistency in the application of the questionnaire, and a 99% response rate. The weaknesses of the study design lie in the potential for inaccurate information to be given over the telephone or recorded afterwards, and for the subject matter of the study to bias the responses. However, such a bias should increase positive responses. The brevity and closed design of the questionnaire sought to minimise all these problems. These results show that most UK units do not premedicate before intubation. Our findings are similar to those of Ziegler and Todres. Reasons were not formally documented, but many commented that there wasn’t time, particularly in an emergency reintubation. This has not been the experience in our unit and only in exceptional cases has it not been possible to ventilate using a bag–valve–mask or T piece while premedication is prepared. All doctors should be able to maintain an airway and hand ventilate after appropriate training. The use of local guidelines and protocols should mitigate any anxiety over the use of potent sedative and anaesthetic drugs by junior doctors. In practice, elective intubations by inexperienced juniors should be supervised and emergency intubations are likely to be performed by a more experienced operator. Barrington and Byrne have recently reported on the safety and practicability of premedicating 253 neonates for intubation, using a regimen of atropine, fentanyl, and suxamethonium, in a unit with the variable skill mix and experience that is inevitable in daily practice.

In those units that do premedicate, morphine remains the most popular choice. This may be due to familiarity, although the wide range of doses of morphine recorded in table 4 suggests that some operators use homeopathy to avoid prolonged respiratory depression while others use much larger doses to try to accelerate the slow onset of effect. However, there are several drugs that are better than morphine in terms of speed of onset, duration of effect, and side effect profile. Fentanyl and alfentanil are potent opioids with a rapid onset and short duration of action when given as a bolus. Barrington’s regimen, using fentanyl 3–4 mcg/kg produced chest wall rigidity as the only side effect in just 4/253 neonates and three resolved promptly with the administration of suxamethonium. This side effect seems to be related to peak plasma concentration and can be minimised by slow bolus administration.

Diazepam has a rapid onset of action and causes little haemodynamic or respiratory depression in isolation, but it and its active metabolites have long half lives. Midazolam is less problematic in this respect, but has been reported to be associated with myoclonic activity when given as a bolus and possibly with fits in preterm neonates when given too rapidly.

Of the induction agents, propofol is widely used before intubation in children and infants, although there are no published data on experience in neonatal units. Ketamine offers cardiorespiratory stability but may raise intracranial pressure, which makes it less suitable. Barbiturates are not widely used, although methohexitone has been studied. They are rapidly effective but have prolonged elimination half lives.

Only 22% of units using any sedation also used neuromuscular blockade before intubating. Encouragingly, all muscle relaxants were accompanied by sedation. Most units used a short acting agent. Suxamethonium is still the most rapidly acting relaxant available and has important safety benefits in clinical practice where variations in skill and experience are inevitable. Friesen stated that premedication did not coadminister a vagolytic drug to pre-empt the potential profound bradycardia that may be associated with suxamethonium, especially if given more than once. We did not enquire whether a vagolytic was drawn up ready in these nine units.

Currently 63% of UK neonatal units give no sedation before intubation on their unit. Only 14% have a protocol for premedication before intubation and only 8% use it for elective and emergency reintubations on the unit. This is despite an increasing body of research which supports this practice, on the grounds that it helps to maintain physiological homeostasis, may mitigate against risk factors for intraventricular haemorrhage, and reduces the time taken to intubate. There is also no evidence that sedation before intubation is less appropriate in neonates than in adults and children, in whom awake intubation would not be tolerated. While further studies are necessary to establish the optimal drug regimen and doses, there is sufficient evidence to support the routine practice of neonatal premedication prior to elective intubation.

Commentary

It is impossible to intubate an awake adult without adequate analgesia or sedation; attempts to do so produce a variety of undesirable and sometimes harmful pathophysiological responses. In contrast, awake intubation of a neonate remains common practice, despite mounting evidence that it is painful, stressful, and potentially damaging.

Some neonatal units now use anaesthetic or analgesic drugs before laryngoscopy, but it is clear from the article by Whyte et al. that there is no consensus on this. A reluctance to use anaesthesia might be because of fears that the drugs themselves could be harmful, or that it is not feasible to give these drugs in acute care.

Duncan et al. have reviewed the published data on neonatal intubation, and it is clear that amnistration of sedative, analgesic, or anaesthetic drugs can make intubation easier to perform and also avoid the hypoxia and haemodynamic consequences associated with awake intubation. However, two issues are unclear. First, which is the most appropriate drug or drugs for elective neonatal intubation, and secondly, what techniques are available for the neonate requiring semi-urgent intubation in the delivery room. It is surprising that despite the current interest in neonatal sedation and analgesia, so few data are available on the provision of effective analgesia and anaesthesia for neonatal intubation.

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