<table>
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<th><strong>Alert</strong></th>
<th>High risk medication - may cause significant patient harm when used in error</th>
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| **Indication** | Analgesia/sedation  
-during assisted ventilation and/or after operative surgery  
-premedication prior to intubation or other procedure |
| **Action** | Narcotic analgesic - stimulates brain opioid receptors |
| **Drug Type** | Narcotic analgesic |
| **Trade Name** | DBL Morphine sulphate injection |
| **Presentation** | Morphine 10mg/mL (10,000 microgram/mL) vial |
| **Dosage / Interval** | **CONTINUOUS IV INFUSION**  
5-40 microgram/kg/hour  
**IV BOLUS**  
50 microgram/kg every 4 hours  
**PRE-MEDICATION FOR INTUBATION**  
100 microgram/kg as a single dose |
| **Maximum Daily Dose** | No extra benefit noted using dosage more than 20 microgram/kg/hour. Doses up to 100 microgram/kg/hour have been used in newborns, however an increase in morphine infusion rate by 10 microgram/kg/hour was associated with an increase in the duration of mechanical ventilation by 24 hrs. |
| **Route** | IV |
| **Preparation/Dilution** | **SINGLE STRENGTH** continuous IV infusion  
| Infusion strength | Prescribed amount |
| 1mL/hour = 20 microgram/kg/hour | 1 mg/kg morphine and make up to 50mL |
| **DOUBLE STRENGTH** continuous IV infusion  
| Infusion strength | Prescribed amount |
| 1mL/hour = 40 microgram/kg/hour | 2 mg/kg morphine and make up to 50mL |
| **IV BOLUS** | Draw up 1mL (10mg) and add 9mL Sodium Chloride 0.9% to make final volume of 10mL with a concentration of 1mg/mL |
| **PRE-MEDICATION FOR INTUBATION** | As above for IV bolus. Wait at least 5 minutes for onset of action after giving the dose, however for maximum effect wait 15 minutes after giving the dose. |

**Administration**  
CONTINUOUS IV INFUSION: via syringe driver, change infusion solution every 48 hours.  
**IV BOLUS:** administer over 5 minutes. Flush with 1mL sodium chloride 0.9% before and after injection. Rapid IV administration may increase adverse effects  
**PRE-MEDICATION FOR INTUBATION:** as above for IV bolus. Wait at least 5 minutes for onset of action after giving the dose, however for maximum effect wait 15 minutes after giving the dose.
### Monitoring

Observe for signs of respiratory and cardiac depression - continuous cardio-respiratory monitoring mandatory. Respiratory depression / apnoea can be reversed with Naloxone

Observe for urinary retention, abdominal distension or delay in passage of stool.

Withdraw slowly following prolonged use.

### Contraindications

Hypersensitivity to morphine sulphate or any component

### Precautions

Use with caution in patients with hypersensitivity reactions to other opioids.

Hypotension and bradycardia

Transient hypertension.

Ileus and delayed gastric emptying time.

Urine retention.

Respiratory depression

Tolerance may develop after prolonged use - wean slowly.

Convulsions

Renal or hepatic impairment

### Drug Interactions

Use with other CNS depressants potentiates effects of opioids, increasing risk of respiratory depression, profound sedation or coma

### Adverse Reactions

See Precautions

### Compatibility

Fluids: Glucose 2.5%, 5% and 10%, glucose in sodium chloride solutions, Hartmann’s, Ringer’s, sodium chloride 0.45% and 0.9%

Y site administration: Adrenaline hydrochloride, amifostine, amikacin, amiodarone, ampicillin, anidulafungin, atracurium, atropine, aztreonam, bivalirudin, caspofungin, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, cephalixin, chloramphenicol, cisatracurium, clindamycin, dexamethasone, digoxin, dopamine, doripenem, eptifibatide, erythromycin, esmolol, filgrastim, fluconazole, foscarnet, gentamicin, granisetron, haloperidol lactate, hydrocortisone, hyoscine hydrobromide, insulin (short-acting), ketorolac, lactobacillus, levomepromazine, lignocaine, linezolid, lorazepam, magnesium sulfate, methylprednisolone sodium succinate, metoclopromide, metoprolol, metronidazole, midazolam, milrinone, noradrenaline, palonosetron, pancuronium, piperacillin-tazobactam (EDTA-free), potassium chloride, remifentanil, sodium nitroprusside, tacrolimus, tigecycline, tirofiban, tobramycin, trimethoprim-sulfamethoxazole, vancomycin, vecuronium, zidovudine

### Incompatibility

Fluids: Morphine may precipitate out of solution when the final pH is greater than 6.4.

Drugs: Aminophylline, azathioprine, azithromycin, flucloxacillin, folic acid, ganciclovir, indomethacin, pethidine, promethazine, sodium nitrite, thiopentone

### Stability

Discard ampoule and unused portion after initial use (Schedule 8 Drug)

### Storage

Store below 25°C

Protect from light.

Discard remainder after use.

S8 medication. Store in DD (Dangerous Drugs) safe and record use in DD register.

### Special Comments

Prolonged use (>5–7 days) may be associated with dependence

### Evidence summary

Dosing

A dose of 10 micrograms/kg/hour is recommended by a systematic review and meta-analysis of 13 studies of ventilated neonates[7], a retrospective review examining age and infusion rates[8] and a 5 year outcome of a large RCT using low dose morphine[9]. In addition, hypotension is not a side effect of morphine when low doses are used[10].

A prospective study of 68 neonates who underwent non-cardiac surgery measured morphine plasma concentrations and comfort scores during postoperative management. A doses of 5–7 micrograms/kg/h for neonates 7 days or less and 10 micrograms/kg/h for neonates over 7 days was recommended[11].
Although the pharmacokinetics of morphine differs in premature infants in regards to the ratio of M3G to M6G metabolites formation, there appears to be no clinical advantage in using higher dose regimen (20)

Effectiveness

As there is no strong evidence for using morphine in ventilated neonates but it is recognised that ventilation is a painful procedure. It was recommended that Opioids should be used selectively with ventilated neonates based on clinical judgements and evaluation of pain indices [7](PIPP-R, PAT).

Several studies identified morphine as safer than midazolam for sedating ventilated neonates and for post-operative management morphine is safer than both fentanyl and midazolam. When used with IV paracetamol the morphine clearance was better over 48 hours[12]

Several studies [13, 14] indicated that continuous infusion of morphine does not alleviate procedural pain and they recommend an alternate such as sucrose be used for these procedures. In addition morphine should be used with caution in non-intubated neonates[15]

The use of morphine for tracheal intubation is unclear. In a published review of 14 surveys of practice there were multiple groups of medications used for premedication for elective intubation[16]. However the author indicates that there is sufficient evidence for stress and pain to support some use of premedication.

Level of evidence

Morphine should be used selectively based on clinical judgement and the use of a validated pain score. (Level A, Grade A)
A dose of Morphine 10 micrograms/kg/hour is recommended for ventilated neonates. (Level A, Grade A)
For postoperative management the recommended doses are 5-7 micrograms/kg/h for neonates 7 days or less and 10 micrograms/kg/h for neonates over 7 days (Level B, Grade B)
A premedication regime be decided and used for all elective intubation. (Level C, Grade C)

References

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