

DEXTA

Guidance on Morphine Dose Reduction

Site training aid

1. Purpose

This guidance provides standardised instructions for reducing morphine infusions in babies enrolled in DEXTA when pain score and other clinical assessments indicate adequate comfort. Pain score should be measured using the Neonatal Pain Agitation and Sedation Scale (N-PASS).

This guidance aims to ensure safe and consistent practice across all trial sites. It MUST be used in conjunction with local clinical guidelines. This is a proposed guidance to be used only while the baby is receiving the 120-hour infusion of the DEXTA investigational medicinal product (IMP).

2. Background

The aim of the study, DEXTA, is to investigate if giving dexmedetomidine, with morphine, to mechanically ventilated preterm babies, can reduce the amount of morphine needed to provide adequate analgesia. Babies participating in the trial will be given a 120-hour infusion of the IMP (dexmedetomidine or a matching placebo) alongside morphine for analgesia. If the baby is comfortable, the morphine dose will be reduced (and can be stopped) and if they are in pain, morphine dose will be increased. This will enable us to find out if babies who were receiving dexmedetomidine needed less morphine as compared to those who were receiving the placebo.

3. Pain assessment and other monitoring during the IMP infusion

- Assess heart rate (RR), respiratory rate (RR), oxygen saturation (SaO₂), and oxygen given as FiO₂ continuously and make hourly recordings.
- Assess and record blood pressure (BP) at least every 2 to 4 hours.
- Assess pain every 2 to 4 hours using N-PASS.
- A score between -5 and +3 indicates the baby is comfortable.
- Use clinical judgment in conjunction with NPASS to guide decisions.

4. Principles of Morphine dose changes

1. The aim of adequate analgesia is to keep babies comfortable without giving excess morphine.
2. Total N-PASS scores of -5 to +3 indicate that baby is comfortable. Score >3 suggest pain and <-5 suggest deep sedation. These scores should be combined with other clinical assessments for pain and baby's clinical condition in making decisions about changes in morphine dose.

3. Morphine infusion rate can be reduced if N-PASS score indicates that baby is comfortable (NPASS total score -5 to +3) and there are no other clinical concerns that suggest pain or discomfort.
4. For each reduction step, reduce infusion rate by 20-25% for e.g., if a baby is on 20 microgram/kg/hour morphine infusion, reduce to 15 microgram/kg/hour (reduction by 25%).
5. If the baby is already on the lowest possible infusion rate of morphine, and the pain assessment (N-PASS and other clinical assessments) show baby is comfortable, morphine infusion can be stopped.
6. Morphine infusion rate can be reduced (or infusion stopped as in point 2) if N-PASS score suggests deep sedation (total score <-5) unless there are clinical indication to keep the baby in deep sedation e.g., immediate post-operative period.
7. Morphine infusion can be restarted or rate increased and a bolus dose considered if the N-PASS score is >3 and other clinical assessments suggest baby is in pain/discomfort.
8. Rate can be increased by 20-25% following a bolus of 50 to 100 microgram/kg morphine but larger infusion rate increments may be needed if baby is in severe pain. The reduction rate and bolus dose are suggestions, follow local guidance as required.
9. Repeat N-PASS score and other clinical assessment of comfort within 2 hours of every dose change. Reduce or increase morphine as required following each assessment.

5. Documentation

- Record all clinical observations (N-PASS total score, HR, RR, SaO₂, FiO₂ and BP) and transcribe to the Case Report Form. If these observations are routinely recorded in clinical notes, they can be transcribed into the eCRF later.
- Record hourly infusion rates (in ml/hour) and strength of the morphine solution and enter into the eCRF
Record date/time of any change in infusion rate and the reason for the change in infusion rate

Summary

- Ensure baby receives adequate analgesia without excess morphine.
- Assess N-PASS every 2 to 4 hours.
- If baby is comfortable or over sedated, reduce morphine dose.
- If baby is in pain or uncomfortable, increase morphine dose.
- Continue monitoring and document all changes and reason for making the change.