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DEXTA

DEXmedetomidine Trial of Adjunct Treatment with Morphine

IMP

DEXTA

NHS
University Hospitals of Derby and Burton
NHS Foundation Trust

FUNDED BY
NIHR | National Institute for Health and Care Research

NOTTINGHAM CLINICAL TRIALS UNIT
at the University of Nottingham

Purpose of the training

Who are these slides for?

- This condensed slide deck provides essential Good Clinical Practice (GCP) guidance for bedside staff who will be preparing, administering and disposing of the DEXTA IMP. It is your responsibility to ensure participant safety, trial integrity and compliance with regulatory and protocol requirements.

- You are not required to review the whole SIV slides. Instead, please review these slides and the DEXTA IMP manual. Please ensure you are signed off on the training and delegation log before commencing any DEXTA IMP activity.

- These set of slides will cover the following:
  - GCP principles
  - Basic Trial Information
  - IMP Background, Preparation & Administration

GCP principles

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GCP Principles

Participant safety

- The rights, safety, and well-being of DEXTA participants take precedence over all other considerations.
- **Discuss any safety concerns with the site DEXTA PI, a member of the local research team, or the DEXTA team at the NCTU as soon as possible.**
- Ensure that any death or Serious Adverse Event (SAE) of a DEXTA participant is reported to your local research team and the local PI as soon as possible. The investigator will ensure that the SAE is submitted within 24 hours of becoming aware of the event
- The trial is not collecting expected SAEs (if in doubt discuss with the site PI) these are:
  - Known complications of prematurity, dexmedetomidine or morphine
  - Events listed as trial outcomes.

GCP Principles

Participant safety: SAEs

An **SAE** is = any untoward medical occurrence or effect that:

- Results in death
- Is life threatening
- Requires hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant disability or incapacity
- Is a congenital anomaly/birth defect
- Or is otherwise considered medically significant by the Investigator

Comments: The term severe is often used to describe the intensity (severity) of a specific event.

This is not the same as serious, which is based on participants/event outcome or action criteria.

GCP Principles

Follow the approved protocol

- The DEXTA IMP should be prepared and administered exactly as specified in these slides and the IMP manual, according to the DEXTA protocol.
- The IMP doses should be given according to the prescription.
- Any deviations from the DEXTA protocol or GCP requirements should be reported as a protocol deviation to the DEXTA team.

GCP Principles

Accurate documentation

- Please record administered doses of the IMP using your sites drug chart.

- Any unused ampoules should be returned to pharmacy. The pharmacy team will then document the disposal of unused ampoules in the DEXTA accountability log.

Trial information

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Trial background

Why we are doing the trial

- Pain management in ventilated preterm babies is often **not well managed or well researched**.
- **Morphine and fentanyl** are the drugs most commonly used to manage pain in ventilated newborns but they may:
  - **not always relieve pain effectively**
  - **slow breathing and feeding**, and delay coming off the ventilator
  - **affect long-term brain development**
- **Dexmedetomidine (dexmed)** is a newer medicine already used in adults and children and it may:
  - Provide effective pain relief with fewer side effects compared to opiates
  - Reduce the amount of morphine babies need

Trial details

Trial groups

The trial is split into three arms:

High dose dexmed (0.5mcg/kg/hr) + morphine

OR

Low dose dexmed (0.25mcg/kg/hr) + morphine

OR

Placebo + morphine

IMP

IMP Pack Information

Dexmed

- The IMP will be supplied in blinded ampoule pairs with identical packaging.
- The ampoules will be 2ml glass ampoules
- Each kit contains 7 pairs of ampoules, only 5 will be needed for the infusion
- There are 2 spares ampoules to allow for spillage / breakage
- **Please read the DEXTA IMP manual as part of your IMP and safety training**

outer carton (measuring 6.5 × 10.5 × 2.9 cm)

IMP Pack Configuration

Ampoule pairs

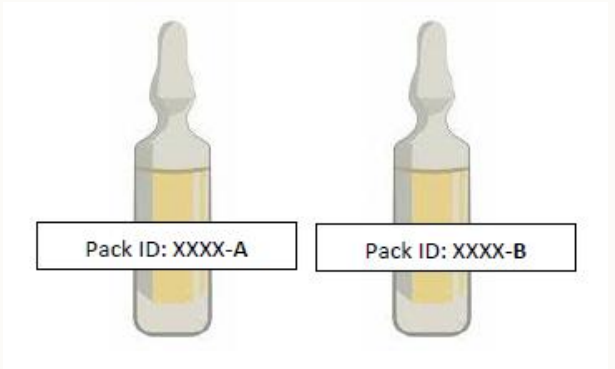
Below are the ampoule configurations for each treatment group.

Treatment group	How supplied (blinded)	Participant kit presentation
DexmedeTOMIDine 0.25 micrograms/kg/hr	Each pair of ampoules: 1 x DexmedeTOMIDine 100 micrograms/ml ampoule 1 x Placebo ampoule	Each kit contains 7 pairs of ampoules
DexmedeTOMIDine 0.5 micrograms/kg/hr	Each pair of ampoules: 2 x DexmedeTOMIDine 100 micrograms/ml ampoule 0 x Placebo ampoule	Each kit contains 7 pairs of ampoules
Control	Each pair of ampoules: 0 x DexmedeTOMIDine 100 micrograms/ml ampoule 2 x Placebo ampoule	Each kit contains 7 pairs of ampoules

IMP Preparation

Preparation

- The pack ID will be provided as soon as randomisation is complete. The pack ID will ensure that blinding is maintained.
- Please double check the **pack ID** on the IMP pack prior to preparation
- Use the ampoule pair (A + B) according to the baby's weight band
- Dilute with 5% Glucose or 0.9% sodium chloride
- Use immediately after preparation (IV syringe should be changed every 24h)



IMP Dilution

Dilution differences

Using aseptic technique, prepare a 50mL infusion syringe according to the baby's working body weight as follows:

For babies with a working body weight of **less than 800 grams**:

- Withdraw **0.25 mL from ampoule A**
- Withdraw **0.25 mL from ampoule B**
- Add **49.5** mL of diluent (Glucose 5% or Sodium Chloride 0.9%)

For babies with a working body weight of **≥ 800 grams**:

- Withdraw **0.5 mL from ampoule A**
- Withdraw **0.5 mL from ampoule B**
- Add **49 mL** of diluent (Glucose 5% or Sodium chloride 0.9%)

IMP Infusion Rate Chart

Infusion rate for babies with working body weight less than 800 grams

Preparation: 0.25mL Ampoule A + 0.25mL Ampoule B + 49.5mL diluent

Body weight	Half rate (mL/hr)	Full rate (mL/hr)
450 - 469 grams	0.11	0.23
470 - 489 grams	0.12	0.24
490 - 509 grams	0.12	0.25
510 - 529 grams	0.13	0.26
530 - 549 grams	0.13	0.27
550 - 569 grams	0.14	0.28
570 - 589 grams	0.14	0.29
590 - 609 grams	0.15	0.30
610 - 629 grams	0.15	0.31
630 - 649 grams	0.16	0.32
650 - 669 grams	0.16	0.33
670 - 689 grams	0.17	0.34
690 - 709 grams	0.17	0.35
710 - 729 grams	0.18	0.36
730 - 749 grams	0.18	0.37
750 - 769 grams	0.19	0.38
770 - 789 grams	0.19	0.39
790 - 799 grams	0.20	0.40

Infusion rate for babies with working body weight ≥ 800 grams

Preparation: 0.5mL Ampoule A + 0.5mL Ampoule B + 49mL diluent

Body weight	Half rate (mL/hr)	Full rate (mL/hr)
800 - 849 grams	0.10	0.20
850 - 899 grams	0.11	0.21
900 - 949 grams	0.11	0.23
950 - 999 grams	0.12	0.24
1 - 1.09 kg	0.13	0.25
1.1 - 1.19 kg	0.14	0.28
1.2 - 1.29 kg	0.15	0.30
1.3 - 1.39 kg	0.16	0.33
1.4 - 1.49 kg	0.18	0.35
1.5 - 1.59 kg	0.19	0.38
1.6 - 1.69 kg	0.20	0.40
1.7 - 1.79 kg	0.21	0.43
1.8 - 1.89 kg	0.23	0.45
1.9 - 1.99 kg	0.24	0.48
2 - 2.09 kg	0.25	0.50
2.1 - 2.19 kg	0.26	0.53
2.2 - 2.29 kg	0.28	0.55
2.3 - 2.39 kg	0.29	0.58
2.4 - 2.49 kg	0.30	0.60
2.5 - 2.59 kg	0.31	0.63
2.6 - 2.69 kg	0.33	0.65
2.7 - 2.79 kg	0.34	0.68
2.8 - 2.89 kg	0.35	0.70
2.9 - 2.99 kg	0.36	0.73
3 - 3.09 kg	0.38	0.75
3.1 - 3.19 kg	0.39	0.78

IMP Administration

Administration

- Begin the infusion when the baby is at least 168 hours old and as close to randomisation as possible.
- The infusion can begin at any time during the day. This will count as day 1.
- Infuse at half the target rate for the first 24 hours then follow the titration guide
- Follow titration guide for pain and haemodynamic stability (this is provided in the **IMP manual**)

IMP Y site compatibility

Y site compatibility

- Compatible with: adrenaline, atracurium, caffeine citrate, calcium gluconate, morphine, etc.
- Not compatible with: amphotericin B, diazepam, ketamine
- Separate infusion preferred for TPN, fat emulsion, sodium bicarbonate
- Full compatibility list is available in the appendix of the IMP manual

IMP Dose Modification

Dose modification and infusion guide

- A flowchart to guide IMP and morphine rate titration is provided in the **IMP manual**.
- There is also a **morphine reduction guidance document** that will be shared as part of the training pack that sites can use if they would like further guidance about how to reduce morphine levels.
- Tables are provided in the IMP manual to ensure clinical staff know exactly at what rate they should be infusing according to the baby's weight.

IMP Returns and Recall

Return and recall procedures

- Used ampoules after IMP preparation needs to be discarded as per local waste policies
- Unused ampoules after the 5-day infusion period will need to be returned to pharmacy where it will be logged.
- Any damaged packs, please quarantine and notify CTU immediately.
- If the CTU has been notified of a drug recall. Recall instructions will be disseminated to site as soon as possible

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Thank you

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