University Hospital of North Staffordshire NHS
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Guidance for Intranasal Diamorphine for the Management of Pain in Children

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Intranasal diamorphine for the management of pain in children

Background

- Methods of giving analgesia to children are imperfect, particularly for those with moderate to severe acute pain. Oral analgesia is often inadequate due to limitations in drug choice and delayed gastric emptying. Intramuscular and intravenous injections can distress young people and rectal administration has limited acceptability.

- Giving drugs via the nasal route is well described and has several advantages. The nasal mucosa is richly vascularised and venous drainage avoids first pass metabolism problems. Diamorphine is highly soluble in water facilitating preparation at high concentrations and a small volume can be used promoting absorption transmucosally without major leakage down the back of the nose and subsequent swallowing. Potency of diamorphine is about twice that of morphine with similar onset and duration of action and equivalent pharmacokinetic profiles of the nasal and intramuscular administration routes of diamorphine has been shown.

Licensed Indications

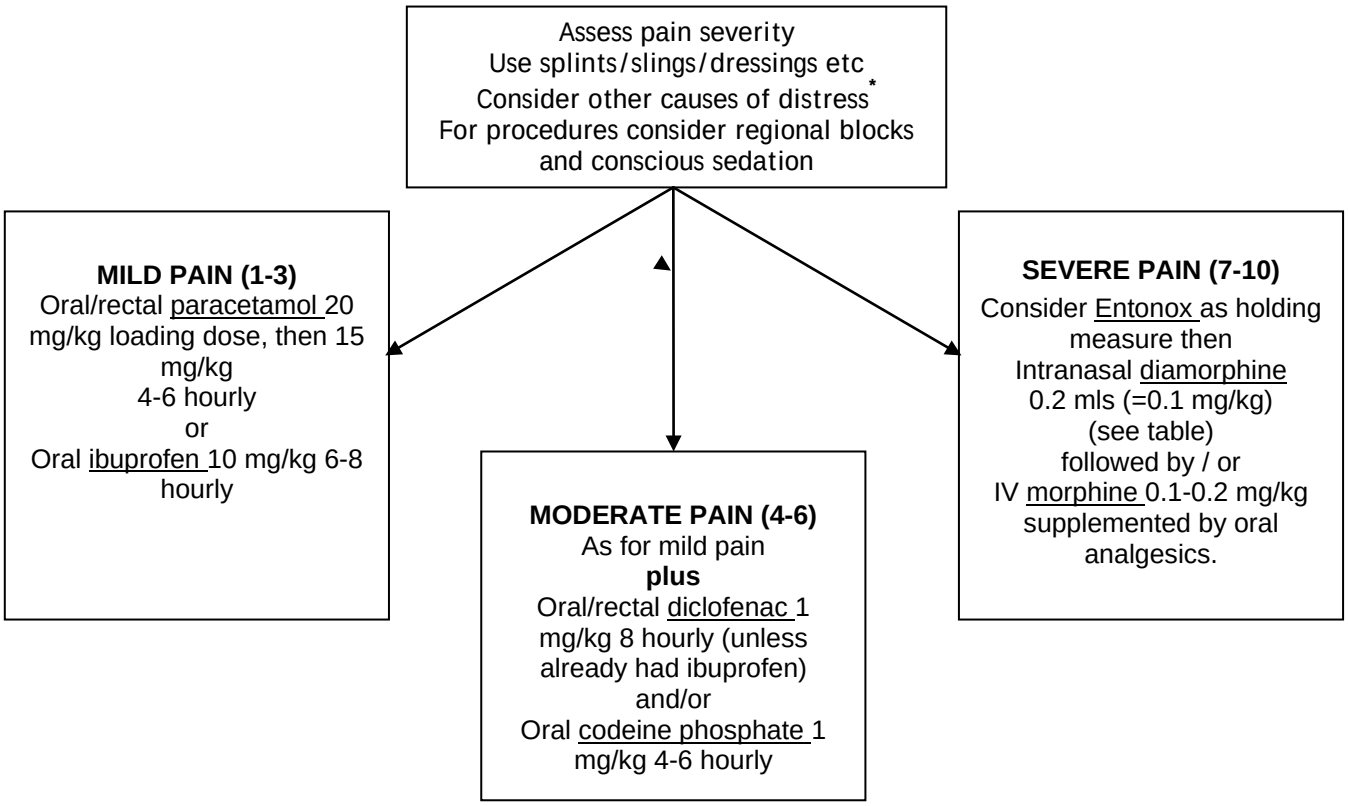
- The use of intranasal diamorphine for this indication would be in an 'off-label' manner. Diamorphine ampoules would be used which are licensed for *im* or *iv* injections in pain management and would be administered via a Mucosal Atomisation Device intranasally.

NICE and other guidance

- There is no current NICE guidance.

- The **British Association for Emergency Medicines'** clinical effectiveness committee have produced a guideline for the management of pain in children.[1.] In this guideline. In the treatment of pain, psychological strategies, non-pharmacological adjuncts and pharmacological agents should be utilised. An algorithm covering the recommended drugs and routes of choice was produced in 2004.

Algorithm from BAEM Guideline for the Management of Pain in Children:[1.]



*Other causes of distress include: fear of the unfamiliar environment, parental distress, fear of strangers, needle phobia, fear of injury severity etc.

For the use in the management of acute/severe pain in children within the emergency care centre by senior medical staff who have been trained appropriately in its use.

For acute pain intranasal diamorphine should be prepared as follows:

1. Dilute 10mg of diamorphine powder with the specific volume of Sterile Water

Child's weight	Volume of Sterile Water
10 Kg	1.9 mL
15 Kg	1.3 mL
20 Kg	1.0 mL
25 Kg	0.8 mL
30 Kg	0.7 mL
35 Kg	0.6 mL
40 Kg	0.5 mL
50 Kg	0.4 mL
60 Kg	0.3 mL

2. Instil 0.2 mL of the solution into one nostril using a 1mL syringe (gives 0.1mg/Kg in 0.2mL).

Notes:

- The classification of pain recommended within the guideline is based on the Wong Baker & APLS ladder pain score scales.
- Patients who have received intranasal diamorphine only require monitored observation for 20 minutes after administration. Children who fall into the moderate-severe pain categories should also be given basic analgesia.
- In all cases it is important to consider the use of non-pharmacological techniques to achieve analgesia whenever possible.

Efficacy

- There are 2 key trials to support the use of intranasal diamorphine.

- Wilson *et al* evaluated the safety and efficacy of intranasal diamorphine as an analgesic for use in children within A&E departments in a small, unblinded trial.[2] This was a prospective, randomised clinical trial including 58 children between the ages of 3 and 16 years, all with suspected limb fractures. Patients were randomised to either intranasal diamorphine (0.1mg/Kg) or intramuscular morphine (0.2mg/Kg). Pain scores, Glasgow coma scores and peripheral oxygen saturations were recorded at 0, 5, 10, 20 and 30 minutes and parental acceptability was assessed at 30 minutes.

  Complete data was obtained for 51 (88%) of the participants. The median summed decrease in pain score was better for intranasal diamorphine than intramuscular morphine however, this was not significant ($p=0.4$). The treatment episode was recorded as 'acceptable' in all parents whose child received intranasal diamorphine compared with only 55% of parents in the intramuscular morphine group ($p<0.0001$). In the study there was no incidence of decrease peripheral oxygen saturation or depression in the level of consciousness in any patient.

- Kendall *et al* undertook a multicentre randomised controlled trial of single dose diamorphine nasal spray compared to intramuscular morphine for the management of acute pain in children and teenagers with clinical fractures presenting to A&E departments.[3] Patients between 3 and 16 years were eligible for inclusion and those excluded were patients present without an accompanying parent or guardian, head injury patients, any patients with a need for immediate intraveneous access, blocked nose or upper respiratory tract infection, learning difficulties, blindness or visual impairment, previous participation in the study, opioid analgesia in the preceeding 2 days and contraindications to diamorphine or morphine.

  Diamorphine was administered at a dose of 0.1mg/Kg in 0.1mL delivered via a nasal dosing device. Morphine sulphate was given at doses of 0.2mg/Kg by

intramuscular injection. After 20 minutes of administration, if the patient was in severe pain the leading clinician could give rescue analgesia of intramuscular morphine (0.2mg/Kg). The primary outcome measure the study assessed were the effectiveness of pain relief, and secondary ones included the patients' reaction to administration and the acceptability of the treatment by parents.

Pain assessments were taken at baseline and at 5, 10, 20 and 30 minutes using Wong Baker face pain scales or a visual analogue scale. At the time of treatment the nurse recorded patient's reaction to administration in one of five categories: *no obvious discomfort, mild reaction, winced or withdrew, cried* or *screamed.* The nurse also described the acceptability of the treatment as *acceptable, stressful, very stressful* or *unacceptable.* A similar assessment was made by the parent or guardian at 30 minutes. Patients assessments were done at each time point included presence of adverse effects, pulse, respiratory rate, oxygen saturation and Glasgow coma scale.

412 patients were included in the trial, 9 of which were subsequently excluded.

Effectiveness: both groups had similar distributions of Wong Baker face pain scores at the time of treatment (*p=0.77*), which improved in both groups during the study duration. Onset of action was quicker in the intranasal diamorphine group, shown by statistically significant differences in the pain scores between 5 and 20 minutes, however at 30 minutes there was no difference (*p=0.20*). The need for rescue analgesia did not differ in either group.

Patient's reaction to treatment: patients reacted worse to the intramuscular injection than the nasal spray. Overall 80% of patients given intranasal diamorphine showed no obvious discomfort compared with only 9% of the intramuscular group (*p<0.0001*). Conversely 3% of patients screamed or cried when given the spray compared with 50% when given intramuscular morphine.

Acceptability of treatment administration: treatment was judged 'acceptable' by staff in 98% of patients in the spray group compared with 32% in the intramuscular injection group (*p<0.0001*). Acceptability by parents after 30 minutes was also statistically greater with the spray than the intramuscular injection (97% *vs.* 72%, *p<0.0001*).

No difference was seen for pulse, respiratory rate and Glasgow coma scores between the groups at any time. Although not clinically significant oxygen saturation was slightly lower at 5, 10 and 20 minutes, with no difference at 30 minutes. No unexpected adverse effects were seen. One person in the intramuscular group had nausea and vomiting which recovered spontaneously. Overall 84 non-serious adverse reactions occurred all of which were mild except for one in the intranasal group that was considered severe (abdominal pain and vomiting).

Dosage Forms

- Diamorphine presents as ampoules of powder ready for reconstitution. This should be reconstituted as directed on attached protocol dependent on the child's weight.

Cost analysis

- Current cost per 10mg vial of diamorphine is £2.87. Any remaining solution once reconstituted would be destroyed therefore each dose of intranasal diamorphine would remain at £2.87. The cost of the atomiser needs to be included in the total cost of administration. Birmingham Children's Hospital use a mucosal atomiser device which is available through normal logistics deliveries and costs £61.85 for a box of 25.

References

1. BAEM. Guideline for the management of pain in children, 2004. Accessed via www.emergencymed.org.uk on 11.08.08
2. Wilson *et al*. Intranasal diamorphine for paediatric analgesia: assessment of safety and efficacy. *Journal of Accident and Emergency* 2004; **14(2)**: 70-72
3. Kendall *et al*. Multicentre randomised controlled trial of nasal diamorphine for analgesia in children and teenagers with clinical fractures. *BMJ* 2001; **322**: 261-65.

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