Intranasal diamorphine for paediatric analgesia: assessment of safety and efficacy

Jason A Wilson, Jason M Kendall, Paul Cornelius

Abstract

Objective—To evaluate the safety and efficacy of intranasal diamorphine as an analgesic for use in children in accident and emergency (A&E).

Methods—A prospective, randomised clinical trial with consecutive recruitment of patients aged between 3 and 16 years with clinically suspected limb fractures. One group received 0.1 mg/kg intranasal diamorphine, and the other group received 0.2 mg/kg intramuscular morphine. At 0, 5, 10, 20, and 30 minutes pain scores, Glasgow coma score, and peripheral oxygen saturations were recorded; parental acceptability was assessed at 30 minutes.

Results—58 children were recruited, with complete data collection in 51 (88%); the median summed decrease in pain score was better for intranasal diamorphine than intramuscular morphine (9 v 8), though this was not significant (P = 0.4, Mann-Whitney U test). The 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, Fisher's exact test). There was no incidence of decreased peripheral oxygen saturation or depression in the level of consciousness in any patient.

Conclusions—Intranasal diamorphine is an effective, safe, and acceptable method of analgesia for children requiring opiates in the A&E department.

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Keywords: intranasal analgesia; children; diamorphine.

Analgesia in the paediatric population is still imperfect, especially for children with moderate to severe pain. Difficulties arise because of limitations in the available therapeutic armoury, routes of administration, and challenges with communication.

Oral analgesia may be inadequate because of drug choice (paracetamol) or delayed gastric emptying. Intramuscular administration can distress the child, as can intravenous administration, which is also often restricted by nursing protocols. The rectal route suffers from limited acceptability, problems of slow and variable onset, and consent, particularly in unconscious patients.'

Administration of drugs through the nasal mucosa is well described12 and is attractive for a number of reasons. The nasal mucosa is richly vascularised and the subepithelial cells are lined by a fenestrated epithelium. The vascular drainage is through the facial and sphenopalatine veins so drugs avoid first pass metabolism in the gut and the liver. Patient acceptability is high when compared with the rectal and intramuscular/intravenous routes of administration.

Diamorphine has a number of properties which render it desirable as an analgesic agent for administration by the transmucosal nasal route. It is rapidly and well absorbed across the nasal mucosa due to its lipophilicity; high aqueous solubility allows administration in a small volume, and it has a low irritancy. It has a potency twice that of morphine, with a similar duration of action. It is widely available in the United Kingdom, familiar to many doctors, and is inexpensive.

Diamorphine given by the intranasal route has not yet been described as an analgesic for children, although other opioids have been given in this way under different circumstances (for example, fentanyl3 and meperidine4 for postoperative pain relief).

Methods

The aim of the study was to evaluate the safety and efficacy of intranasal diamorphine as an analgesic for use in children, by comparing it with intramuscular morphine sulphate, an accepted standard. The study design (a prospective, randomised trial with consecutive recruitment of patients) was approved by the Frenchay NHS Healthcare Trust ethics committee.

Consecutive children presenting to the accident and emergency (A&E) department of Bristol Frenchay Hospital from January to September 1995, between the ages of 3 and 16 years, with a clinically diagnosed limb fracture, were recruited into the study. Patients with head injuries, nasal obstruction, and injuries requiring immediate intravenous access were excluded.
Table 1 Intranasal diamorphine dose schedule

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Volume (of saline in ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>1.3</td>
</tr>
<tr>
<td>20</td>
<td>1.0</td>
</tr>
<tr>
<td>25</td>
<td>0.8</td>
</tr>
<tr>
<td>30</td>
<td>0.7</td>
</tr>
<tr>
<td>35</td>
<td>0.6</td>
</tr>
<tr>
<td>40</td>
<td>0.5</td>
</tr>
<tr>
<td>50</td>
<td>0.4</td>
</tr>
<tr>
<td>60</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Notes:
1. Obtain weight of child (to nearest 5 kg).
2. Add appropriate volume to a 10 mg ampoule of diamorphine.
3. Draw up 0.2 ml of solution for intranasal use.

Outcome measures were as follows:
(1) Analgesic efficacy: reduction in pain scores as recorded on visual analogue scales, and Wong Baker faces.
(2) Parental acceptability, categorically graded by direct questioning.
(3) Occurrence of unwanted side effects, particularly respiratory depression and depression of level of consciousness.

Informed, written consent was obtained from one parent and witnessed oral consent (where appropriate) was obtained from the child.

Consecutive patients who fulfilled the inclusion criteria were randomised according to their hospital number to receive either intranasal diamorphine (0.1 mg/kg), or intramuscular morphine sulphate (0.2 mg/kg).

The type of injury was recorded.

Intranasal diamorphine was always given in a volume of 0.2 ml; the concentration of diamorphine in this volume varied with the weight of the child according to the dose schedule (table 1). It was given using a 1 ml syringe resting in one nostril with the patient reclining in a position of comfort. The 0.2 ml of solution was allowed to drop gently into the patient’s nostril.

Intramuscular administration was by conventional technique. Both routes of administration were performed by the nursing staff.

Pain scores were measured using Wong Baker faces (in the children aged between 3 and 8) and visual analogue scales (in the children aged between 8 and 16). There were six faces ranging from happy to sad, which were numbered from 1 to 6, and the visual analogue scale was divided into six equal segments and numbered from 1 to 6. This allowed subsequent comparisons across all age groups.

All patients had baseline pain scores recorded at time zero, just before the administration of analgesia, and subsequent measurements at 5, 10, 20, and 30 minutes postanalgesia. All patients had peripheral oxygen saturations measured by continuous pulse oximetry and observations of their Glasgow coma score (GCS) at each assessment point. They did not receive supplemental oxygen treatment.

Rescue analgesia (intramuscular morphine sulphate) was offered at 30 minutes if required.

Parents were asked to decide whether the whole episode was “unacceptable”, “stressful”, or “acceptable”.

To compare analgesic efficacy, a single summary statistic was calculated for each patient

Table 2 Demographic details

<table>
<thead>
<tr>
<th>Intranasal diamorphine</th>
<th>Intramuscular morphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>30</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>7.4</td>
</tr>
<tr>
<td>Baseline median pain score (95% CI)</td>
<td>*4 (3 to 5)</td>
</tr>
</tbody>
</table>

* Not significant (Mann-Whitney U).

Table 3 Median decrease in pain scores (with 95% confidence intervals of medians)

<table>
<thead>
<tr>
<th>Intranasal diamorphine</th>
<th>Intramuscular morphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>t = 5 min</td>
<td>1 (0 to 2)</td>
</tr>
<tr>
<td>t = 10 min</td>
<td>2 (1 to 3)</td>
</tr>
<tr>
<td>t = 20 min</td>
<td>3 (1 to 3)</td>
</tr>
<tr>
<td>t = 30 min</td>
<td>3 (2 to 4)</td>
</tr>
<tr>
<td>Summed medians</td>
<td>g*</td>
</tr>
</tbody>
</table>

* Not significant (P = 0.4, Mann-Whitney U).

Discussion
The aim of this study was to evaluate the safety and efficacy of intranasal diamorphine. It was compared with morphine sulphate, which is particularly respiratory depression and depression of level of consciousness.

Informed, written consent was obtained from one parent and witnessed oral consent (where appropriate) was obtained from the child.

Consecutive patients who fulfilled the inclusion criteria were randomised according to their hospital number to receive either intranasal diamorphine (0.1 mg/kg), or intramuscular morphine sulphate (0.2 mg/kg).

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Rescue analgesia (intramuscular morphine sulphate) was offered at 30 minutes if required.

Parents were asked to decide whether the whole episode was “unacceptable”, “stressful”, or “acceptable”.

To compare analgesic efficacy, a single summary statistic was calculated for each patient
proved especially popular
analgesia
reports
scoring
pain
no
peripheral
oxygen
were no
diamorphine
Intranasal
current
methods
chosen for
muscular
level
low
0.1
was
ated with
syringe
and needle would
effective and
children in
administration.
This
is
diamorphine
impossible;
Therefore this is a
relatively low dose, but it was used for reasons
of safety in this first study in children.

We have shown that 0.1 mg/kg of intranasal
diamorphine is as effective as 0.2 mg/kg intra-
muscular morphine in the 3-16 year age group
with clinically diagnosed limb fractures, and we
encountered no unwanted side effects: there
were no recorded episodes of decreased
peripheral oxygen saturation or depression of
the level of consciousness. This puts an upper
limit on the likelihood of either event happen-
ing in a population receiving intranasal
diamorphine at 10% with a confidence limit of
95%. The under 3 year olds were not
included in the study because compliance with
pain scoring would have been impossible; there
is no reason, however, why intranasal diamor-
phine should not be just as effective in this age
group.

Many medical and nursing staff are reluctant
to administer intramuscular analgesia for
children in pain because of the perceived distress a
syringe and needle would cause the child.
Intranasal diamorphine seemed to be
associated with good compliance, with no parental
reports of a “stressful” or “unacceptable”
patient episode. This route of administration
has proved especially popular among the nurs-
ing staff, who are now unwilling to give
intramuscular analgesia to this population.

Intranasal diamorphine has advantages over
current methods of paediatric analgesia. It is
effective and can be administered by nursing
staff, it does not involve needles and syringes, it
has a rapid onset, and there are no problems
related to acceptability (compared with, for
example, rectal administration) or variable
absorption.

There is a significant proportion of paediat-
ric patients who experience moderate to severe
pain whose analgesic needs are poorly met;
paracetamol is inadequate but their care givers
are reluctant to use intravenous or intramuscu-
lar opiates because of perceived distress to the
child. Intranasal diamorphine offers effective,
rapid, potent analgesia with no patient distress.

It is now used routinely at Frenchay
Hospital, and we are widening the indications
for its use (for example, to include finger tip
injuries, small burns, etc). The next step for us
is a multicentre trial in the South West region
to improve the power of the safety data, so that
its widespread use can be recommended.

CONCLUSION
Intranasal diamorphine seems to be effective
and safe in the treatment of moderate to severe
pain in children, and should be considered as
an analgesic of first choice in patients with
moderate to severe pain who do not require
immediate intravenous access. It offers the
potential for a significant improvement in paed-
diatric analgesic practice.

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Hammersmith Hospital), and C Doré (Department of Medical
Statistics, Hammersmith Hospital) for their statistical advice.

1 Mitchell J, James MA, Lunn JN. A fundamental problem of
2 Karl FW, Keiffer AT, Rosenberger JL, Larach MG, Ruffle
JM. Comparison of the safety and efficacy of intranasal
midazolam or suftanilat for preinduction of anaesthesia in
3 Walberg EJ, Wills RJ, Eckert J. Plasma concentrations of
midazolam in children following intranasal administration.
4 Cauna N, Hindere KH. Fine structure of blood vessels of
the human respiratory mucosa. Ann Otol Rhinol Laryngol
1969;78:865.
5 Williams PL, Warwick R, eds. Gray’s anatomy, 36th ed.
6 Cone EJ, Holicky BA, Grant TM, Darwin WD, Goldberger
BA. Pharmacokinetics and pharmacodynamics of intrana-
7 Robinson SL, Rowbotham DJ, Smith G. Meperine
compared with diamorphine: A comparison of dose require-
ments and side effects after hip surgery. Anaesthesia 1991;
46:538—40.
8 Striebel HW, Pommerening J, Rieger A. Intranasal fentanyl
titration for postoperative pain management in an unse-
9 Striebel HW, Maliewcz J, Hermans K, Castello R. Intrana-
sal meperidine titration for postoperative pain relief.
11 Huskisson EC. Measurement of pain. Lancet 1974;i:
1127—31.
12 Hanley JA, Lippman-Hand A. If nothing goes wrong, is eve-
ything all right? Interpreting zero numerators. JAMA
1983;249:1743—5.
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