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ORIGINAL ARTICLES

Intranasal diamorphine for paediatric analgesia: assessment of safety and efficacy

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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.

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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.[1]

Administration of drugs through the nasal mucosa is well described[2,3] and is attractive for a number of reasons. The nasal mucosa is richly vascularised and the subepithelial cells are lined by a fenestrated epithelium.[4] The vascular drainage is through the facial and sphenopalatine veins[5] 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[6]; 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.[7] 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, fentanyl[8] and meperidine[9] 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

Weight (kg)	*Volume (of saline in ml)*
15	1.3
20	1.0
25	0.8
30	0.7
35	0.6
40	0.5
50	0.4
60	0.3

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.[10] 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).[11] 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 (the median summed decrease in pain score). This was calculated by summing the difference from baseline of each pain score for each of the four post analgesia time points. The medians and 95% confidence limits for the medians were calculated for the intranasal diamorphine and intramuscular morphine sulphate groups. Groups were compared using the Mann-Whitney U test. A P value of 0.05 was taken as being statistically significant.

Table 2 Demographic details

	Intranasal diamorphine	*Intramuscular morphine*
Number	30	22
Mean age (years)	7.4	7.9
Baseline median pain score (95% CI)	*4 (3 to 5)	*5 (3 to 6)

* Not significant (Mann-Whitney U).
CI, confidence interval.

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

	Intranasal diamorphine	*Intramuscular morphine*
t = 5 min	1 (0 to 2)	1 (0 to 1)
t = 10 min	2 (1 to 3)	2 (1 to 2)
t = 20 min	3 (1 to 3)	2 (1 to 3)
t = 30 min	3 (2 to 4)	3 (2 to 3)
Summed medians	9*	8*

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

Results

Data collection was complete, allowing subsequent analysis, in 51 out of 58 patients (88%). In the other seven patients, data were incomplete because of child non-compliance with pain scoring or inadequate data collection by staff.

The pattern of injuries was comparable in both groups (the majority of patients having fractures of the radius and ulna), and there was no significant difference in the mean age between the groups (table 2). Table 2 also shows the baseline pain scores. There was no significant difference between the groups.

Table 3 and the figure show the median decrease in the pain scores: the intranasal diamorphine group showed a larger change in the median summed decrease than the intranasal morphine group (9 *v* 8), though this was not significant (P = 0.4, Mann-Whitney U analysis).

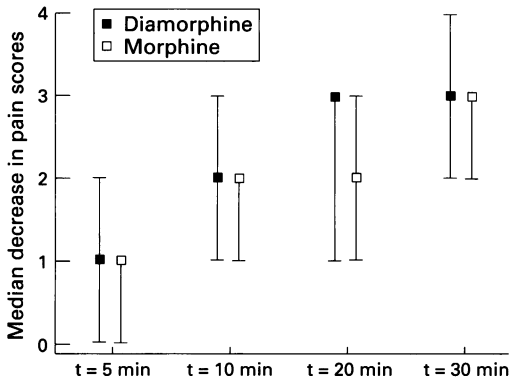
One patient who received intranasal diamorphine and one patient who received intramuscular morphine required rescue analgesia.

There was no episode of decreased peripheral oxygen saturation or depression of GCS in either group.

Parental acceptability was significantly better in the intranasal diamorphine group: all of the intranasal diamorphine group described the episode as "acceptable", compared with only 55% of the intramuscular morphine group (P < 0.0001, Fisher's exact test).

Discussion

The aim of this study was to evaluate the safety and efficacy of intranasal diamorphine. It was compared with morphine sulphate, which is



Median decrease in pain scores.

the gold standard. As both drugs were to be given by nursing staff the intramuscular route was chosen for morphine administration.

The intranasal diamorphine dose chosen was 0.1 mg/kg, which is equivalent to the "standard" intramuscular dose; prior work in adults suggests a 50% bioavailability for intranasal administration.[6] 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 intramuscular 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 happening in a population receiving intranasal diamorphine at 10% with a confidence limit of 95%.[12] 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 diamorphine 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 nursing 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 paediatric 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 intramuscular 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 paediatric analgesic practice.

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1 Mitchell J, James MA, Lunn JN. A fundamental problem of consent. BMJ 1995;310:43—6.
2 Karl HW, Keiffer AT, Rosenberger JL, Larach MG, Ruffle JM. Comparison of the safety and efficacy of intranasal midazolam or sufentanil for preinduction of anaesthesia in paediatric patients. Anaesthesiology 1992;76:209—15.
3 Walbergh EJ, Wills RJ, Eckhert J. Plasma concentrations of midazolam in children following intranasal administration. Anaesthesiology 1991;74:233.
4 Cauna N, Hinderer 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. Edinburgh: Churchill Livingstone, 1980.
6 Cone EJ, Holicky BA, Grant TM, Darwin WD, Goldberger BA. Pharmacokinetics and pharmacodynamics of intranasal "snorted" heroin. J Anal Toxicol 1984;17:327—37.
7 Robinson SL, Rowbotham DJ, Smith G. Morpine compared with diamorphine. A comparison of dose requirements 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 unselected population. Anaesthesia 1993;48:753—7.
9 Striebel HW, Malewicz J, Hermanns K, Castello R. Intranasal meperidine titration for postoperative pain relief. Anesth Analg 1993;76:1047—51.
10 Mygind N. *Conventional medical treatment. Nasal allergy.* Oxford: Blackwell Scientific Publications, 1979:257.
11 Huskisson EC. Measurement of pain. Lancet 1974;ii: 1127—31.
12 Hanley JA, Lippman-Hand A. If nothing goes wrong, is everything all right? Interpreting zero numerators. JAMA 1983; 249:1743—5.