Continuous papaveretum infusion for the control of pain in painful sickling crisis

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Abstract

We describe our experience of using continuous papaveretum infusions to control pain in 24 children admitted on 45 occasions with painful sickling crisis. The children were aged from 1.7 to 14.3 years. Infusion duration ranged from one to nine days (median three days), total dose from 0.3 to 21 mg/kg (median 2.4 mg/kg), with a pronounced tendency for dosage to increase with increasing age. No respiratory depression was observed. One infusion was discontinued because of cerebral toxicity.

It is well recognised that analgesia for children is frequently underprescribed and under-administered.^{1 2} For children intramuscular injections can themselves be a source of pain and apprehension.² The use of opiate infusions for children with postoperative or terminal pain is now well established.³⁻⁵ Children with sickle disease may suffer repeated episodes of severe pain during sickling crises. The standard treatment for these is hydration and analgesia.⁶ Analgesia is often delivered in the form of intermittent intramuscular opiates, although there is increasing use of opiate infusions.⁶⁻⁸ In 1988 we introduced continuous papaveretum infusions as the preferred method of providing analgesia for severe sickling crisis.

Patients and methods

Over 18 months, 24 children aged 1.7 to 14.3 years presented with severe sickling crisis on 45 occasions. Eighteen had homozygous sickle cell disease, four had sickle cell haemoglobin C disease, and two sickle/β° thalassaemia. On 19 occasions the site of pain was in the limbs, on 11 occasions in the back or abdomen, and on 15 in multiple sites. None of these children fulfilled the exclusion criteria listed below and all received a papaveretum infusion.

PROTOCOL

A papaveretum infusion was administered to any child with a sickling crisis sufficiently painful to warrant opiate analgesia, excluding any with the following disorders: (i) pre-existing respiratory depression secondary to pulmonary or neurological problems or (ii) active cholecystitis and biliary colic.

The infusion was made up as papaveretum 1 mg/kg in 60 ml of dextrose saline solution and delivered via a syringe driver. A 3 ml bolus (50 µg/kg) was given initially and the rate set at

3 ml/hour for the first hour. Nursing staff assessed the level of pain hourly and adjusted the infusion rate to keep the child pain free or comfortable, usually between 2 ml/hour and 6 ml/hour (33-100 µg/kg/hour). Higher rates were used occasionally after discussion with medical staff. When pain was abolished the rate was gradually reduced, and an oral analgesic such as paracetamol was administered before the infusion was discontinued.

Respiratory rate was recorded hourly and conscious level was monitored informally.

In a subgroup of 11 children aged 4.5 to 12.2 years the effectiveness of analgesia was evaluated using a five point pain analogue scale (see fig 1).⁹ The scale was explained to the child and then he/she was asked to grade the severity of the pain hourly while awake. This score was used by nursing staff in their evaluation of pain.

Results

There was wide variation in the duration of the infusions (see table 1). During most painful episodes (n=30) infusions were given for one to three days, but a small number (n=6) required continuing intravenous analgesia for five to nine days. Variation in dosage was also wide with more than half of the infusions peaking at a daily dose in excess of the standard recommended dose (0.9 mg/kg daily, derived from 150 µg/kg every four to six hours). Although no individual patterns could be discerned, there was a pronounced trend for older children to receive higher doses (per kg) and infusions of longer duration (see fig 2). This correlation reached significance for both maximum hourly rate and maximum daily dose.

There was some variation in dosage between children with different haematological diagnoses, children with sickle/β° thalassaemia requiring higher doses than children with homozygous sickle cell disease or sickle cell haemoglobin C disease, but these observations are based on small numbers.

The results of the subgroup of 11 children evaluated by the pain analogue scale are shown in table 2. The dosage and duration of infusion in this group did not differ from the group as a whole. Pain scores varied widely with 50% of children pain free for at least 44% of the hours studied, and with moderate to severe pain for less than 12% of the time. In contrast other children had moderate to severe pain for up to 37% of the hours studied and were pain free for as little as 17% of the time.

No respiratory toxicity was observed. Most of the patients were tachypnoeic on admission,

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Face	Severity of pain	Numerical score
No pain (no hurt)	0
Very mild pain (a little hurt)	1
Mild pain (a bit more hurt)	2
Moderate pain (a big hurt)	3
Severe pain (a very big hurt)	4
Very severe pain (the worst hurt you can imagine)	5

For each child, the nurse ascertained his/her vocabulary for pain and using the appropriate words (examples in brackets) described the faces to the child and asked him/her to choose the one which best expressed the child's degree of pain.

Figure 1 Description of the 'faces' pain scale used with younger children.

Table 1 The duration and dosage of papaveretum infusions in 45 episodes of painful sickling crisis. Results given as range (median)

Age (years)	No of episodes	Duration of infusion (days)	Maximum rate* ($\mu\text{g/kg/hour}$)	Maximum dose† (mg/kg/day)	Total dose‡ (mg/kg)
0-5	18	1-6 (2)	30-130 (60)	0.3-2.1 (0.9)	0.3-7.2 (1.5)
5-10	17	1-9 (3)	40-140 (68)	0.5-3.4 (1.3)	0.7-10.9 (2.4)
10-15	10	2-8 (3)	48-180 (100)	0.5-4.3 (1.5)	0.8-21.1 (2.9)
Total	45	1-9 (3)	30-180 (70)	0.3-4.3 (1.3)	0.3-21 (2.4)
Correlation§		+0.26	+0.43	+0.44	+0.32
p Value		<0.1	<0.005	<0.005	<0.05

*Maximum rate: highest hourly rate/kg of each papaveretum infusion.

†Maximum dose: highest daily dose/kg of papaveretum given during each infusion.

‡Total dose: total dose/kg of papaveretum given during a single admission.

§Correlation: correlation coefficient of age plotted against dose and duration.

Figure 2 The highest daily dose/kg of papaveretum given during each infusion plotted against the patients' age. Correlation coefficient +0.44, $p < 0.005$.

Table 2 Age of patients, dose of papaveretum, and pain chart scores for episodes monitored by pain charts

	Range (median)		
Age (years)	4.5-12.2 (7.3)		
Maximum dose/day (mg/kg/day)	0.5-3.4 (1.6)		
Total dose (mg/kg)	0.5-10.9 (3.3)		
Duration (days)	1-9 (4)		
No of hours chart used	18-126 (48)		
Score	0	1-2	3-5
Range (median) % of time when pain score was as shown*	17-83 (44)	16-80 (39)	0-37 (12)

*Number of hours when pain score = 'n' ÷ number of hours pain charts used × 100.

with a subsequent fall in respiratory rate. Neurological toxicity was seen on one occasion in a 10 year old boy. The infusion was discontinued because of appreciable drowsiness and an alteration in conscious level, which resolved over 12 hours after stopping the infusion. This occurred when he was receiving a dose of 1.3 mg/kg/day. He had previously received 2 mg/kg/day and 2.3 mg/kg/day without ill effect.

Discussion

It is recognised that prescription and administration of analgesics for children is often inadequate when compared with adults.¹ Continuous opiate infusion provides a strategy for ensuring the delivery of analgesic medication to children without relying on painful intramuscular injections.² Experience with continuous opiate infusions is most extensive in the postoperative setting, where its safety is well established. Dilworth and MacKeller describe more than 600 consecutive opiate infusions in children with only seven episodes of respiratory depression, all resolving with reduction of the infusion rate without naloxone.⁵ Minor toxicity, such as nausea and vomiting, occurred in 25%, a similar proportion to that experienced with other postoperative analgesic regimes.

The efficacy of analgesia is most frequently assessed by using a linear analogue scale to describe the degree of pain. Pain score data from comparative studies in adults and children show a consistent improvement in the quality of analgesia delivered by continuous opiate infusion compared with 'as required' or regular intramuscular injections of the same drugs.^{4 10 11} Several studies have shown that higher doses of analgesic are delivered to patients on continuous infusions compared with those receiving intermittent medication.^{4 11} Taken together with data on analgesic administration patterns in children,¹ this suggests that part of the mechanism for better analgesia may be that continuous infusion overcomes the habitual underadministration of analgesia for children. That this is not the entire explanation may be inferred from a comparative study in adults in which the total dose of analgesia was significantly lower in the continuous infusion group by a factor of two to three, but this group also had significantly lower scores on a pain analogue scale.¹⁰

The use of continuous opiate infusions in children with terminal malignancy is an accepted

method of providing analgesia. In the study of Miser *et al* there was considerable variation in dosage, with most patients experiencing adequate analgesia with standard doses of morphine, but two patients required considerably higher doses.³

Experience with continuous opiate infusions in painful sickling crisis is increasing.⁶⁻⁸ In the series of Cole *et al* there was a fivefold variation in maximal dose with a mean of 2.4 mg/kg/day of morphine.⁷

In our series the most striking feature was the extremely wide interindividual and intra-individual variation in dosage, both during and between episodes. In most patients pain was well controlled with doses of 1.3 mg/kg/day (median) but a small number needed substantially higher doses. We observed a consistent increase of dosage per kg with age. This was felt to reflect the increasing severity of painful sickling crises with age, although a better ability to express pain may have played a part.

Pain charts were used prospectively in a selected group to adjust the rate of infusion. The scores obtained can also be used as a measure of the efficacy of analgesia, and they confirm the impression that adequate analgesia was easily achieved in the majority, but required increasing analgesia for several days in a minority. There was no difference in the amount of papaveretum given to children using and not using pain charts but numbers were small and selection was not random so the effects of using pain charts on dosage cannot be fully assessed.

Toxicity is a major limiting factor with opiates given by any route particularly if high doses are used. We observed no respiratory

depression but one episode of neurological toxicity necessitated interruption of the infusion. This episode was not dose related and was thought to represent an idiosyncratic reaction. It serves to underline the importance of monitoring the conscious level in all children on opiate infusions at whatever dose.

In summary, sickling crises vary in severity and duration requiring a flexible approach in providing analgesia. Continuous intravenous infusion of papaveretum provides a flexible means of delivering continuous analgesia which is acceptable to patients and relatively simple to administer. It should therefore be considered as the preferred method of providing analgesia in severe sickling crisis.

1 Schechter NL, Allen DA, Hanson K. Status of paediatric pain control: a comparison of hospital analgesic usage in children and adults. *Pediatrics* 1986;77:11-5.

2 Choonara IA. Pain relief. *Arch Dis Child* 1989;64:1101-2.

3 Miser AW, Miser JS, Clark BS. Continuous intravenous infusion of morphine sulphate for control of severe pain in children with terminal malignancy. *J Pediatr* 1980;96:930-2.

4 Bray RJ. Postoperative analgesia provided by morphine infusion in children. *Anaesthesia* 1983;38:1075-8.

5 Dilworth NM, MacKeller A. Pain relief for the pediatric surgical patient. *J Pediatr Surg* 1987;22:264-6.

6 Evans JPM. Practical management of sickle cell disease. *Arch Dis Child* 1989;64:1748-51.

7 Cole TB, Sprinkle RH, Smith SJ, Buchanan GR. Intravenous narcotic therapy for children with severe sickle cell pain crisis. *Am J Dis Child* 1986;140:1255-9.

8 Davies SC, Brozovic M. The presentation, management and prophylaxis of sickle cell disease. *Blood Reviews* 1989;3:29-44.

9 Wong D, Barker C. Facing pain: how much does a child hurt? *Pediatric Nursing* 1988;1:9-17.

10 Rutter PC, Murphy F, Dudley HAF. Morphine: controlled trial of different methods of administration for postoperative pain relief. *Br Med J* 1980;1:12-3.

11 Church JJ. Continuous narcotic infusions for relief of postoperative pain *Br Med J* 1979;1:977-9.