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Burns 31 (2005) 831–837

BURNS

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Intranasal fentanyl is an equivalent analgesic to oral morphine in paediatric burns patients for dressing changes: A randomised double blind crossover study

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Abstract

Introduction: The ideal analgesic agent for burns wound dressings in paediatric patients would be one that is easy to administer, well tolerated, and produces rapid onset of analgesia with a short duration of action and minimal side-effects to allow rapid resumption of activities and oral intake. We compared our current treatment of oral morphine to intranasal fentanyl in an attempt to find an agent closer to the ideal.
Methods: A randomised double blind two-treatment crossover study comparing intranasal administration of fentanyl (INF) to orally administered morphine (OM). Children with burn injury aged up to 15 years and weighing 10–75 kg were included. Primary end-point was pain scores. Secondary end-points were time to resumption of age-appropriate activities, time to resumption of fluid intake, sedation and cooperation. Routine observations and vital signs were also recorded.
Results: Twenty-four patients were studied with a median age of 4.5 years (interquartile range 1.8–9.0 years) and a median weight of 18.4 kg (interquartile range 12.9–33.2 kg). Mean pain difference scores (OM-INF) ranged from −0.500 (95% CI = −1.653 to 0.653) at baseline to −0.625 (05% CI = −1.863 to 0.613) for a retrospective rating of worst pain experienced during the dressing procedure. All measurements were within a pre-defined range of equivalent efficacy. The median time to resumption of fluid intake was 108 min (range 44–175 min) with OM and 140 min (range 60–210 min) with INF. These differences were not statistically significant. Fewer patients experienced mild side-effects with INF compared to OM ($n = 5$ versus $n = 10$). No patients experienced depressed respirations or oxygen saturations.
Summary: Intranasal fentanyl was shown to be equivalent to oral morphine in the provision of analgesia for burn wound dressing changes in this cohort of paediatric patients. It was concluded that intranasal fentanyl is a suitable analgesic agent for use in paediatric burns dressing changes either by itself or in combination with oral morphine as a top up titratable agent.

Keywords: Intranasal fentanyl; Oral morphine; Pediatric burns; Burns dressings

1. Introduction

Following a burn injury many children require daily wound dressing as part of their management. Once any intravenous cannulas have been removed oral morphine is routinely used as an analgesic for these dressing changes. Wound dressing is often exquisitely painful during the procedure although there may be little, if any pain afterwards. Analgesic requirements are commonly underestimated in patients with burns particularly during these dressing procedures.

The ideal analgesic agent for wound dressings should be easy to administer, be well tolerated by the child, and produce rapid onset analgesia with a short duration of action and minimal side-effects to allow rapid resumption of activities and oral intake.

Analgesic agents currently used for wound dressings fall short of this ideal agent. Although adequate analgesia during the painful procedure can be achieved, prolonged sedation following the procedure limits the child's ability to eat sufficiently to make up their calorie deficiency and to resume their rehabilitation programme. The child may have many hours a day when they are unable to eat, drink or undertake activities.

Morphine orally has an unpredictable onset and effect in clinical practice. It has well known side-effects of nausea,

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0305-4179/$30.00
doi:10.1016/j.burns.2005.05.001

vomiting and sedation. Oral ketamine can be combined with morphine to achieve adequate analgesia, however ketamine also has side-effects of nausea, vomiting and dysphoria, which may be distressing. A commercially available 50:50 mix of nitrous oxide and oxygen gases (Nitronox® Airliquide Healthcare, Entonox® BOC) may be used but is not tolerated by all patients and is unsuitable for young children, when using self-administering devices.

Fentanyl is an opiate that is rapidly absorbed across mucous membranes and has a short onset and duration of analgesia. Intranasal opiates have been used successfully in the emergency department for analgesia in fractures [1–4] and also for post-operative pain relief [5,6]. Oral transmucosal fentanyl citrate (OTFC) has been used in the emergency department [7] and burns unit [8] setting with good effect. Intranasal fentanyl (INF) has been evaluated in a burns unit with encouraging results as a patient controlled medication [9,10] but no studies have explored its use in the paediatric population.

The primary aim of this study was to determine whether INF is equivalent in analgesic effect to oral morphine (OM) in children with burns during daily dressing changes that are part of their routine care. Secondary aims were to determine whether INF improved patient cooperation, sedation and reduced post-dressing recovery time and side-effects compared to OM.

2. Methods

2.1. Setting and population

The study was conducted in the Burns Unit of the Princess Margaret Hospital for Children, Perth, WA. Inpatients with burns covering more than 10% of body surface area or in specialised areas and requiring daily dressing with oral opiate analgesia cover were invited to take part in the study. Additional inclusion criteria were weight from 10 to 75 kg inclusive, age up to and including 15 years and an expected minimum requirement of two consecutive days of dressings with oral opiate cover. Recruitment occurred between December 2001 and July 2003. Patients were excluded if they had significant burns to the face making intranasal administration difficult, known allergies or intolerance to opiates, or extreme anxiety necessitating use of oral anxiolytics. The hospital's Research Ethics Committee approved the study. Written informed consent was obtained from each child's guardian.

2.2. Design and procedures

The study design was a randomised double blind two-treatment crossover trial. Patients were randomly assigned to receive either OM and intranasal placebo (INP) on day 1 followed by oral placebo (OP) and INF on day 2 or INF and OP on day 1 followed by INP and OM on day 2. We refer to the first treatment sequence as Group A and the second as Group B. Hospital pharmacy staff coordinated the randomisation schedule independent of study investigators.

Fig. 1. Mucosal Atomiser Device®.

Oral and intranasal solutions were prepared by the hospital pharmacy. The intranasal solutions were delivered via an atomiser (MAD® Wolfe Tory Medical Inc.) (Fig. 1) containing either normal saline or a concentrated fentanyl solution (150 μg/mL). The oral solutions contained placebo elixir or morphine 5 mg/mL. The placebo oral solution was manufactured to have a similar bitter taste to oral morphine.

The intranasal (IN) drug dose was calculated to equate to 1.4 μg/kg of fentanyl and allowed for 70% bioavailability of the IN solution in comparison with the intravenous solution [11]. This equates to the standard intravenous (IV) fentanyl dose of 1 μg/kg. The oral drug dose equated to 1 mg/kg of OM.

The oral medication, either morphine or placebo, was administered 60 min prior to commencement of the dressing procedure and the intranasal medication, either fentanyl or placebo, was then administered 15 min prior to the procedure. After the procedure had commenced, further 0.1 mL (15 μg) doses of the intranasal solution (either fentanyl or placebo) were administered every 5 min as required until pain relief was adequate up to a maximum of 3 μg/kg. As the treating nurse was blinded to the active drug, if pain relief was still inadequate during the procedure, 50:50 nitrous oxide/oxygen was offered to any child where appropriate. Following the procedure other simple oral analgesics, e.g. paracetamol, ibuprofen were offered if required as per routine nursing practice.

2.3. Measurements

Pain was the primary end-point for this study. We measured pain using either a numeric rating scale (0–10) or our hospital's standard pain measurement tool, the Princess Margaret Hospital Pain Assessment Tool (PMHPAT). This tool incorporates a ''faces scale'' self assessment tool and a score based on facial expression, position in bed, child's vocalisation and the nurse's assessment of pain (Table 1) [12]. The two scales were chosen as they could be

Table 1
Princess Margaret Hospital pain assessment tool (PMHPAT)

Criteria	Score 0	Score 1	Score 2
Facial expression	Face composed/smiling	Face expressionless (flat affect), face distorted (other than that due to surgery or trauma)	Facial grimace
Position in bed	Lying still/relaxed	Restless holding/guarding wound	Lying rigid thrashing
Sounds	Making normal conversation	Whimpering/grizzling, complaining (not to pain)	Crying/screaming, complaining of pain
Nurses' assessment	No pain/very slight pain	Moderate pain	Severe pain
Self assessment	Face 0 or 1 VAS 0–3	Face 2 or 3 VAS > 3–6	Face 4 or 5 VAS > 6

administered without additional equipment during the procedural phase of the dressing change and together they allowed comparison of pain scores across the age spectrum in a normal paediatric burns unit. Children received education on the appropriate pain tool prior to the trial. Pain was measured at four points in time: immediately prior to receiving the oral medication (baseline), immediately prior to the wound dressing procedure (pre-procedure), upon completion of the wound dressing procedure (procedure-end) and, following the procedure-end rating, a retrospective rating of the worst pain experienced during the procedure (worst).

Secondary end-points for the study were post-dressing recovery time, patient cooperation and patient sedation. Post-dressing recovery time was measured as time to resumption of normal activities and time to first fluid intake. Time to resumption of normal activities was assessed by the treating nurse and determined to be when the child resumed age-appropriate activities [8]. Time to first fluid intake was considered an endpoint as the fasting time required for procedural sedation has been regarded as a significant limitation to the adequate hydration and nutrition of these children. Both times were recorded as the total time (in minutes) from the commencement of the dressing procedure to the relevant event.

Patient cooperation was assessed by the treating nurse using a 5-point scale: 1 = cooperative; 2 = verbal resistance; 3 = some movement, intermittent restraint required; 4 = thrashing movements, continuous restraint required; and 5 = unable to complete procedure without intravenous medication. Cooperation was measured on three occasions as per the first three pain measurements. Sedation was rated on a 10-point scale with descriptive labels given in Table 2.

Table 2
Sedation scale

Awake—fully interacting/playing
Awake—interacting, not enthusiastic
Awake—not interacting
Drowsy—eyes opening spontaneously without prompting
Drowsy—eyes opening spontaneously to noise in room
Sleeping—rouses to quiet voice
Sleeping—rouses to loud voice
Sleeping—rouses to light touch
Sleeping—rouses to firm touch
Deeply sleeping—unable to rouse

The scale is based on the Modified Ramsay Sedation Scale [13] but further modified to allow more differentiation in patient alertness. There were seven measurement times for sedation: baseline, 15 min prior to commencement of the dressing procedure, and 15 min thereafter to 60 min post procedure. In addition, pulse oximetry and respiratory rates were recorded every 15 min from the time of oral medication administration until 1 h after completion of the dressing procedure. Adverse events, including vomiting and nausea, and the need for additional oral simple analgesics were recorded.

2.4. Data analysis

A confidence interval approach was used to test oral morphine and intranasal fentanyl for equivalent analgesic efficacy [14]. This method establishes equivalence by showing that a confidence interval surrounding an estimate of the true difference falls entirely within a pre-defined range of equivalence. The range of equivalence was defined to be zero difference $\pm$ 2 pain scale ratings. This difference was based on a previous study showing a 10 mm (95% CI: 7–12 mm) difference on a 100-mm visual analog scale to be an appropriate equivalence limit [15] and following discussions with hospital nurses and anaesthetists who have used pain rating scales extensively.

Pain difference scores were calculated at the patient level for each of the four rating periods by subtracting the pain rating with INF from the rating with OM. To account for a potential period effect on difference scores, both unadjusted and adjusted (for treatment sequence) results are presented. Power calculations indicated that 26 patients would give 90% power to establish equivalence using 95% confidence intervals and allowing for a standard deviation in pain difference scores of 3.

The Wilcoxon signed ranks test was used to analyse times to fluid intake and resumption of normal activities under morphine compared with fentanyl. Due to the limited range of responses on the cooperation and sedation scales, ratings were dichotomised and reported as frequencies. Differences between the two treatment sequence groups on baseline characteristics and original pain ratings were analysed using the Wilcoxon rank sum test for numeric data and the Chi-squared test of independence for category data. The level of significance for all tests was 0.05.

Table 3
Baseline characteristics and drug doses by treatment sequence (Group A, oral morphine first; Group B, intranasal fentanyl first) and for all patients

Characteristic	Group A	Group B	*P*-value[a]	All patients
Number of patients	14	10	0.54	24
Sex (male)	8 (57%)	9 (90%)	0.17	17 (71%)
Age (years)	3.0 (1.5–9.0)	7.0 (2.8–10.8)	0.11	4.5 (1.8–9.0)
Weight (kg)	14.3 (11.9–29.8)	28.8 (14.1–41.8)	0.06	18.4 (12.9–33.2)
OM dose (mg)	14.5 (12.0–29.8)	29.0 (13.8–41.8)	0.08	18.0 (12.3–33.5)
INF dose (μg)	15.0 (15.0–33.8)	37.5 (15.0–60.0)	0.10	22.5 (15.0–45.0)
IN top up for OM active	7 (50%)	7 (70%)	0.42	14 (58%)
IN top up for INF active	8 (64%)	8 (80%)	0.39	16 (67%)

Data are frequency (percentage) or median (interquartile range). OR, oral morphine; INF, intranasal fentanyl.
[a] Exact two-sided results.

3. Results

Twenty-eight patients were recruited and randomised to one of the two treatment sequences. The study protocol was completed by 24 (17 male, 7 female) patients. Of the four patients who did not complete the study protocol, two withdrew before outcomes were recorded and no outcomes were recorded on a further two patients. These four patients (two from each treatment sequence) could not be included in an intention-to-treat analysis because no data were collected on any of the outcome measures. The characteristics of the 24 patients are summarised in Table 3 according to their treatment sequence group and for the total sample. Group differences in baseline characteristics are discussed below in the context of crossover assumptions.

3.1. Crossover assumptions

Differences between treatments at the patient level (crossover differences) may be biased by a period effect, a period by treatment interaction, or carry-over [16]. Mean period differences for the four pain rating periods, obtained by subtracting for each patient their day 2 from their day 1 pain rating, ranged from 0.17 ± 1.10 at baseline to 0.38 ± 2.98 for worst pain. No mean period difference differed significantly from zero ($P = 0.47$–0.72), indicating the absence of a period effect. Median overall (day 1 + day 2) pain ratings were slightly larger for Group A than for Group B for pre-procedure (6.5 versus 3.8) and slightly smaller for procedure-end (0.5 versus 2.0). This pattern is reflected in the median ratings for sequence group by active treatment given in Table 4. However, Wilcoxon rank sum tests performed on the rating sums ($P = 0.13$–0.67) and the original ratings indicated the absence of a period by treatment interaction. While an approximate 24 h separation between the day 1 and day 2 dressing procedures precluded the possibility of carry-over, differences in baseline characteristics for the treatment sequences (Table 3) may have affected treatment difference scores in ways that are indistinguishable from carry-over. However, baseline characteristics were not substantially associated with intra-patient pain difference scores and unlikely to have caused any bias. Of particular importance is that the end of procedure treatment difference scores were independent of sex ($r = 0.03$), age ($r = -0.05$), and weight ($r = -0.07$).

3.2. Pain

The mean pain difference scores and their 95% confidence intervals are displayed in Fig. 2. The mean at baseline was −0.125 (95% CI = −0.592 to 0.342) and close to zero, as would be expected before the administration of any study medication. The means at pre-procedure and

Table 4
Median pain scores for treatment sequence (Group A, OM first; Group B, INF first) and all patients

Characteristic	Group A ($n = 14$)	Group B ($n = 10$)	*P*-value (exact two-sided)	All patients ($n = 24$)
OM active				
Baseline	0 (0–2)	0 (0–1)	0.75	0 (0–1.8)
Pre-procedure	2.8 (0–5.3)	1 (0–2.5)	0.24	1.5 (0–4.8)
Procedure-end	0 (0–2)[a]	1 (0–1.5)[a]	0.47	0.5 (0–2.0)[b]
Worst	3 (0–5.6)	3 (2–5.9)	0.93	3 (0.3–5)
INF active				
Baseline	0 (0–1)	1 (0–1.3)	0.31	0 (0–1)
Pre-procedure	4.3 (0–6)	2 (1–3.1)	0.47	2.5 (1–5)
Procedure-end	0 (0–4)[a]	1.5 (0.8–2.5)	0.45	1 (0–4)[a]
Worst	5 (0.8–6.3)	2.5 (2–4.5)	0.51	3.5 (2–5.9)

Data are median (interquartile range). OM, oral morphine; INF, intranasal fentanyl.
[a] Missing values for one patient.
[b] Missing values for two patients.

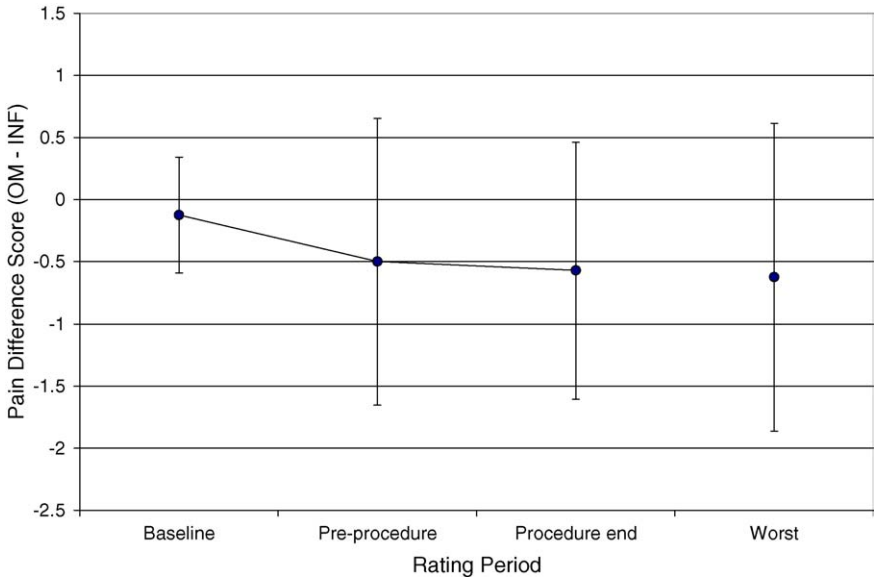


Fig. 2. Mean pain difference scores (OM-INF) and 95% confidence intervals for three rating periods and a retrospective rating of worst pain experienced during the dressing procedure.

procedure-end were, respectively, −0.500 (95% CI = −1.653 to 0.653) and −0.571 (95% CI = −1.605 to 0.462). For the retrospective ratings of worst pain, the mean difference score was −0.625 (95% CI = −1.863 to 0.613). The negative signs indicate that pain ratings tended to be slightly higher with INF than with OM. However, for all rating periods the 95% confidence intervals surrounding mean difference scores fall within the range of clinical indifference defined by zero ± 2. When adjusted for a potential period effect, the mean pain difference scores and their 95% confidence intervals were virtually identical to the unadjusted values. The period adjusted mean at baseline was −0.157 (95% CI = −0.635 to 0.321). The period adjusted mean at pre-procedure and procedure-end times were respectively, −0.550 (95% CI = −1.741 to 0.641) and −0.556 (95% CI = −1.629 to 0.518). For the ratings of worst pain, the adjusted mean difference score was −0.579 (95% CI = −1.859 to 0.702).

3.3. Post-dressing recovery

There were no statistically significant associations between treatment and recovery variables. The median time to fluid intake after wound dressing with OM was 108 min (range = 44–175 min) and 140 min (range = 60–210 min) after INF ($P = 0.37$). The median time to resumption of normal activities was 145 min (range = 55–465 min) after receiving OM compared to a median time of 125 min (range = 70–300 min) after INF ($P = 0.99$).

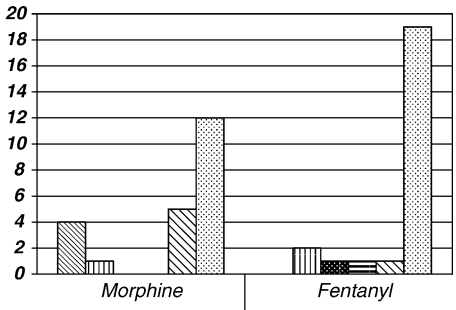
3.4. Cooperation and sedation

A large proportion of patients received a rating of one on the cooperation and sedation scales. We therefore combined response categories by classifying patients as cooperative (rating = 1) versus other (rating > 1) on the cooperation scale and awake and fully interacting/playing (rating = 1) versus other (rating > 1) on the sedation scale. At each rating period for the two scales, ratings were then paired to give two concordant pairs (OM and INF both = 1 or OM and INF both > 1) and two discordant pairs (OM = 1 and INF > 1 or INF = 1 and OM > 1). The number of patients classified in the paired rating categories for the four cooperation and seven sedation rating periods are given in Table 5. It is the discordant pairs that provide information on cooperation and sedation differences between the two opiates. While cooperation was similar with OM and INF across the rating periods, there is a trend in the sedation results indicating that patients became awake and fully interacting/playing earlier with INF compared to OM.

Table 5
Paired ratings of cooperation and sedation with oral morphine (OM) and intranasal fentanyl (INF)

Outcome and time period	Paired ratings[a]			
	Both = 1	Both > 1	OM = 1	INF = 1
Cooperation				
Baseline	13	2	6	3
Pre-procedure	12	5	4	3
Procedure-end[b]	14	1	3	4
Sedation				
Pre (−60)	13	3	3	5
Pre (−15)	12	6	3	3
Procedure	9	8	2	5
Post (+15)	8	7	4	5
Post (+30)[c]	8	4	2	7
Post (+45)[c]	9	5	1	6
Post (+60)[c]	9	4	0	8

[a] 1 = rating of cooperative or awake; >1 = other rating.
[b] Missing values for two patients.
[c] Missing values for three patients.



	Morphine	Fentanyl
Nausea/vomitng	4	0
Drowsy	1	2
Headache	0	1
Abdo cramps	0	1
Itch	5	1
Nil	12	19

Fig. 3. Adverse effects to oral morphine and intranasal fentanyl.

3.5. Adverse effects

Twenty-one percent (5/24) of patients experienced mild side-effects with INF and 42% (10/24) with OM as shown in Fig. 3. The side-effects that were detected in both groups were nausea, vomiting and itching. No patient objected to the intranasal medication and there were no reported episodes of nasal irritation. Only one patient received the 50:50 nitrous oxide/oxygen mixture to inhale and this individual required it on both days of the study. Individual pulse oximetry measurements ranged from 96 to 100% when OM was the active treatment and from 95 to 100% when INF was the active treatment. Median readings ranged from 98.5 to 99% for OM and 98 to 100% for INF. Individual respiratory rates for OM ranged from 16 to 38 min^{-1}, with medians from 22 to 24. The respiratory rates for INF were similar, with individual rates from 16 to 36 min^{-1} and medians from 22 to 24.

4. Discussion

This investigation into the use of intranasal fentanyl for burns dressing changes in children has shown that it provides equivalent analgesia to oral morphine. We were able to demonstrate equivalence in the two agents by comparing the analgesics in similar clinical settings by crossing the patients over from one active opiate to the other over the two consecutive days of the trial. Of interest was the trend in greater alertness and interaction in the group receiving intranasal fentanyl although this did not meet significance.

OM is well known to provide effective analgesia but can have unpredictable absorption and prolonged duration of action [10]. The incidence of side-effects of oral morphine is well known including nausea, vomiting, drowsiness, hypotension, constipation, itch and tolerance. With regular use in dressings these side-effects can prove clinically significant.

Fentanyl is an opiate that has been studied in the setting of burns dressing changes, however, this is the first trial that has compared the intranasal route for administration of the fentanyl to the oral route for the traditional analgesic morphine in the paediatric population. Sharar et al. [8] and Robert et al. [17] used oral transmucosal fentanyl citrate (OTFC) in the management of paediatric burns in small cohorts. The expected fentanyl side-effects are similar to morphine. There is a reported incidence of 20–50% nausea and vomiting with OTFC which reduces its acceptability [7]. The high emesis incidence in the Sharar study reflects the high doses of OTFC which approached 10 μg/kg. Robert et al. compared OTFC with OM in similar patients to our study and found OTFC to be equivalent to OM, but this study was limited to only eight patients and they did not detect side-effects. They did not specifically study the recovery profile of either agent [17].

Irrespective of the route of administration of an opiate monitoring of vital signs and conscious state remains critical to the early detection of adverse incidents. Although the dose range for INF to 3 μg/kg increased the risk of side-effects such as desaturations, nausea and vomiting we did not detect any significant adverse effects. There was a trend to fewer mild side-effects in the INF group in comparison to the OM group.

The intranasal method of administration of opiates was well tolerated by this group of children, and may be related to the atomiser used and the concentrated fentanyl solution allowing smaller volumes of fluid to be administered to the nares. Although the once only administration of an oral medication may be perceived to be less laborious than the use of INF (requiring potentially repeated doses) the OM mixture is quite unpleasant to taste which can make the administration difficult in children. It also requires administration at least 1 h prior to the dressing change. This means that the dressing procedure must be booked in to follow the oral medication after 1 h, which can be difficult in the busy ward. Studies of INF have demonstrated bioavailabilty of 70% with therapeutic levels within 2 min in an adult population [11]. The advantage of the INF is not only its titratability to effect but that the dressing procedure can be commenced shortly after its administration.

We manufactured a concentrated fentanyl solution (150 μg/mL) so as to achieve effective doses while minimising the volume of solution administered to the nares. This concentrated fentanyl solution had been previously studied and shown to be an effective analgesic in the setting of acute pain and reduces the risk of the child swallowing or sneezing out the analgesic [1]. Swallowing the fentanyl reduces its effectiveness as it then passes through the liver and is metabolised.

The IN route offers more flexibility to the nursing staff who can administer repeated doses to titrate against pain. In addition, it has the potential to be used in a patient controlled self-administered manner. A recent study by Finn et al. showed adults could effectively use IN fentanyl for analgesia

in burns dressing changes in a patient controlled manner [10]. In the paediatric setting self-administration would only be reliable in older children.

In our study we did not attempt to enrol the number of burns patients to demonstrate differences in side-effects and recovery profile. Our study was powered to demonstrate equivalent efficacy on the primary outcome and there was no attempt to enrol patients beyond those needed to achieve the primary objective. Ideally a multi-centred study would assist in patient enrolments and allow for significance in the secondary aims.

We used cooperation and sedation scales specially designed to detect clinical states important in the management of burns patients during dressing changes. Although these scales were based on sedation and cooperation scales previously used [8,13], the modifications had not been validated in any other studies. However, they proved to be useful clinical tools for the nursing staff during the procedure.

We used pain scores that were familiar to our nursing staff and simple to use during a dressing procedure even in young children. As an alternative a VAS scale could have been used but we were concerned about difficulties of administering this during the procedure. The VAS has been shown to be an unreliable tool in children less than 8 years [15]. We were keen not to exclude younger children as this constitutes a large percentage of our burns patient population and hence a group that we were most keen to improve options in analgesia.

5. Conclusion

INF has been demonstrated to be as effective as OM in providing pain relief during burns dressing changes. The trend towards improved recovery profile with INF will need confirmation by further larger cohort studies to quantify any advantages. The search for the ideal agent for burns wound dressing remains elusive but INF can be included as an alternative agent in the paediatric population either to be used by itself or in combination with OM as a top up titratable analgesic.

Acknowledgment

This study was funded by the Burns Research Fund at PMH.

References

[1] Borland ML, Jacobs I, Geelhoed G. Intranasal fentanyl reduces acute pain in children in the emergency department: A safety and efficacy study. Emerg Med 2002;14:275–80.
[2] Younge PA, Nichol MF, Kendall JM, et al. A prospective randomised pilot comparison of intranasal fentanyl and intramuscular morphine for analgesia in children presenting to the emergency department with clinical fractures. Emerg Med 1999;11:90–4.
[3] Wilson JA, Kendall JM, Cornelius P. Intranasal diamorphine for paediatric analgesia: assessment of safety and efficacy. J Accid Emerg Med 1997;14:70–2.
[4] Kendall JM, Reeves BC, Latter VS. Multicentre randomised controlled trial of nasal diamorphine for analgesia in children and teenagers with clinical fractures. BMJ 2001;322:261–5.
[5] Toussaint S, Maidl J, Schwagmeier R, et al. Patient-controlled intranasal analgesia: effective alternative to intravenous PCA for postoperative pain relief. Can J Anaesth 2000;47:299–302.
[6] Striebel HW, Olman T, Spies C, et al. Patient controlled intranasal analgesia for the management of postoperative pain: a pilot study. J Clin Anesth 1996;8:4–8.
[7] Schutzman SA, Burg J, Liebelt E, et al. Oral transmucosal fentanyl citrate for premedication of children undergoing laceration repair. Ann Emerg Med 1994;24:1059–64.
[8] Sharar SR, Bratton SL, Carrougher GJ, et al. A comparison of oral transmucosal fentanyl citrate and oral hydromorphone for inpatient paediatric burn wound care analgesia. J Burn Care Rehab 1998;19:16–21.
[9] O'Neill G, Paech M, Wood F. Preliminary clinical use of a patient-controlled intranasal analgesia device. Anaesth Intensive Care 1997;25:408–12.
[10] Finn J, Wright J, Fong J, et al. A randomised crossover trial of patient controlled intranasal fentanyl and oral *morphine* for procedural wound care in adults patients with burns. Burns 2004;30:262–8.
[11] Lim S, Paech M, Sutherland V, et al. Pharmokinetics of nasal fentanyl. J Pharm Pract Res 2003;33:59–63.
[12] Robertson J. Pediatric pain assessment: validation of a multidimensional tool. Pediatr Nurs 1993;19:209–13.
[13] Gill M, Green SM, Krauss B. A study of the bispectral index monitor during procedural sedation and analgesia in the emergency department. Ann Emerg Med 2003;41:234–41.
[14] International Conference on Harmonisation. E9: Guidance on statistical principles for clinical trials. Federal Register 63(179), 16 September 1998.
[15] Powell CV, Kelly AM, Williams A. Determining the minimum clinically significant difference in visual analog pain score for children. Ann Emerg Med 2001;37:28–31.
[16] Senn S. Cross-over trials in clinical research, 2nd ed., Chichester: John Wiley & Sons, 2002.
[17] Robert R, Brack A, Blakeney P, Villareal. et al. A double blind study of the analgesic efficacy of oral transmucosal fentanyl citrate and oral morphine in pediatric patients undergoing burn dressing change and tubbing. J Burn Care Rehab 2003;24:351–5.