2015-06-21

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http://hdl.handle.net/10026.1/3633

PAin SoluTions In the Emergency Setting (PASTIES)—patient controlled analgesia versus routine care in emergency department patients with pain from traumatic injuries: randomised trial

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ABSTRACT

OBJECTIVE

To determine whether patient controlled analgesia (PCA) is better than routine care in patients presenting to emergency departments with moderate to severe pain from traumatic injuries.

DESIGN

Pragmatic, multicentre, parallel group, randomised controlled trial.

SETTING

Five English hospitals.

PARTICIPANTS

200 adults (71% (n=142) male), aged 18 to 75 years, who presented to the emergency department requiring intravenous opioid analgesia for the treatment of moderate to severe pain from traumatic injuries and were expected to be admitted to hospital for at least 12 hours.

INTERVENTIONS

PCA (n=99) or nurse titrated analgesia (treatment as usual; n=101).

MAIN OUTCOME MEASURES

The primary outcome was total pain experienced over the 12 hour study period, derived by standardised area under the curve (scaled from 0 to 100) of each participant's hourly pain scores, captured using a visual analogue scale. Pre-specified secondary outcomes included total morphine use, percentage of study period in moderate/severe pain, percentage of study period asleep, length of hospital stay, and satisfaction with pain management.

RESULTS

200 participants were included in the primary analyses. Mean total pain experienced was 47.2 (SD 21.9) for the treatment as usual group and 44.0 (24.0) for the PCA group. Adjusted analyses indicated slightly (but not statistically significantly) lower total pain experienced in the PCA group than in the routine care group (mean difference 2.7, 95% confidence interval −2.4 to 7.8). Participants allocated to PCA used more morphine in total than did participants in the treatment as usual group (mean 44.3 (23.2) *v* 27.2 (18.2) mg; mean difference 17.0, 11.3 to 22.7). PCA participants spent, on average, less time in moderate/severe pain (36.2% (31.0) *v* 44.1% (31.6)), but the difference was not statistically significant. A higher proportion of PCA participants reported being perfectly or very satisfied compared with the treatment as usual group (86% (78/91) *v* 76% (74/98)), but this was also not statistically significant.

CONCLUSIONS

PCA provided no statistically significant reduction in pain compared with routine care for emergency department patients with traumatic injuries.

TRIAL REGISTRATION

European Clinical Trials Database EudraCT2011-000194-31; Current Controlled Trials ISRCTN25343280.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Pain is common in patients presenting to emergency departments, but it is often not treated effectively

Patient controlled analgesia (PCA) has been shown to be more effective than standard methods of analgesia delivery in other clinical areas, but very limited evidence relating to its use in the emergency setting exists

No previous trials have reported the use of PCA from emergency admission to the hospital ward

WHAT THIS STUDY ADDS

No statistically significant difference was seen in effectiveness between PCA and treatment as usual in emergency patients who are admitted to hospital with pain from traumatic injuries

This is the first study to follow up participants from emergency admission to the hospital ward; it has therefore given a pragmatic answer to the question of whether PCA should be used in these patients

Introduction

Pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage."[1] Pain is the most common reason that patients present to the emergency department, but it is often not treated effectively.[2] In a national survey of emergency department patients, 64% reported that they were in pain.[3] The Royal College of Emergency Medicine recommends that patients in severe pain should receive analgesia within 20 minutes of arrival in the emergency department, with regular reassessment and further action as required.[4] However, effective analgesia is often not achieved, and almost half of patients surveyed thought that more could be done to treat their pain in the emergency department.[3]

Routine care for patients in moderate or severe pain often involves the administration of intravenous morphine, which is the standard opioid used in most hospitals and has been shown to be as effective as other opioids.[5] In emergency departments across the United Kingdom, analgesia for patients in severe pain is provided by nurse delivered intravenous

morphine over several minutes to achieve pain relief. This technique is safe and effective in the short term but places considerable demands on nursing time, particularly when repeated doses are needed.[6]

Once a patient is admitted to a hospital ward, severe pain may be managed using strong oral opioid analgesia or advanced pain management techniques. Best practice includes multimodal analgesia using regular paracetamol and non-steroidal anti-inflammatory drugs, in addition to opioids. The decision to admit a patient to the ward has been shown to delay the delivery of effective analgesia in the emergency department, suggesting that this group of patients are at particular risk of poor pain management.[7]

One solution may be to allow patients to deliver opioid analgesia themselves via a patient controlled analgesia (PCA) device. This device consists of a volumetric pump, which delivers a set intravenous dose of drug when a control button is pressed. The PCA system includes anti-siphon and anti-reflux valves to minimise the risk of inadvertent drug delivery. The pump has a safety "lockout" period when it will not deliver a further dose of opioid. A protocol commonly used throughout many UK hospitals, in settings other than the emergency department, uses a bolus dose of 1 mg morphine and a lockout period of five minutes and is derived from a broad evidence base.[8-11] PCA has been shown to be more effective than standard methods of analgesia delivery in providing pain relief in areas such as postoperative care, burns, and terminal care.[12-15] PCA is most effective in maintaining analgesia once baseline pain relief has been established.[16]

Despite the high prevalence of pain in emergency department patients, evidence relating to the use of PCA in this setting is very limited. Previous studies in this area provide limited evidence of the short term utility of PCA in emergency patients but have not considered the management of pain over the subsequent hours after hospital admission.[17-20] We did not identify any previous or current studies that combine emergency department care with ongoing ward care to assess quality of pain relief beyond four hours, and no detailed analysis of the cost effectiveness of PCA in this setting has previously been reported.

The aim of our study was therefore to compare PCA morphine with routine care (nurse titrated intravenous morphine in the emergency department and oral or parenteral morphine on the wards) in adult emergency patients who present in moderate or severe pain due to traumatic injuries and are then admitted to an inpatient ward.

Methods

The detailed methodology and study protocol are described in a separate protocol paper.[21]

Study design

The study comprised two contemporaneous multicentre, open label, randomised trials of PCA versus routine care in the emergency department. Patients presenting to the emergency department requiring intravenous analgesia and admission to hospital with either traumatic musculoskeletal injury or non-traumatic abdominal pain were potentially eligible for inclusion. Key outcome measures were collected at baseline and then hourly for 12 hours. Although two separate trials were running (one of patients presenting with traumatic musculoskeletal injuries, the other of patients with non-traumatic abdominal pain), both were based on the same protocol, which is outlined below. Nevertheless, we have considered them as two separate trials, as they are powered separately. This paper describes the trial involving patients with traumatic injuries.

Participants

Eligible patients were adults presenting to the emergency department with pain from traumatic injuries requiring intravenous opioid analgesia and hospital admission for at least 12 hours from the time of enrolment. Table 1 lists exclusion criteria.[21] Study participants were patients who met the eligibility criteria and were willing and able to give informed consent.

Recruitment

Patients underwent initial assessment and management, including initial pain relief, according to local policy. A research nurse screened patients on their arrival at the emergency department. After initial assessment and pain management, a research nurse approached patients and gave them an information sheet detailing the study. If they were happy to discuss the study further, any questions were answered at this stage. Patients were then fully assessed against the inclusion and exclusion criteria before written informed consent was obtained from patients willing and able to participate. Patients who declined to take part were not obliged to give a reason, but the research nurse recorded any reasons given.

Study procedures and data collection

After informed consent was obtained, the first study pain score was recorded using a visual analogue scale, and the participant was randomised (using a secure web based randomisation system) to receive either PCA or routine care.

Participants in both groups then received instructions on how to complete subsequent visual analogue scale scores, entering them into a mini flipchart (the participant was instructed to turn the page of the flipchart after an entry was made, so the previous score was not visible for comparison). Electronic timers (Casio F-91W digital watches) issued a bleep every hour as a reminder to the participant to complete the hourly score, but this bleep was not typically loud enough to wake the participant from sleep. The visual analogue scale was presented as a 10 cm horizontal line with verbal anchors at each end of "no pain" and "worst pain possible." Participants were instructed to select the point along the line (and mark this point with a pen with a single vertical line) that reflected their current pain perception. Participants recorded pain scores at 60 minute intervals over a

Table 1 | Exclusion criteria

Criteria	Rationale
Patients over 75 years old	Altered plasma concentrations of opioid in this age group for given standard dose of PCA
Patients with a reduced conscious level (Glasgow coma score <15)	Will not be able to give informed consent
Inability to operate PCA device	Will not be able to complete intervention
Patients who cannot understand study information (for example, owing to pre-existing dementia, learning difficulties, or intoxication)	Will not be able to give informed consent
Patients with chronic pain	Altered pain processing or opioid tolerance
Patients who are opioid tolerant or have active opioid addiction	Abnormal response to opioids or potential opioid misuse
Patients with history of renal failure	Accumulation of active opioid metabolites
Allergy or other contraindication to morphine	
Hypotension (systolic blood pressure <90 mm Hg)	Morphine may exacerbate hypotension
Patients in police custody or in prison	
Inability to gain intravenous access	Will not be able to receive intravenous morphine
Patients who are likely to be definitively treated in ED and discharged or who are likely to require transfer for surgery direct from ED	Will not be able to complete 12 hours of visual analogue scale scoring
Patients who are pregnant or breast feeding	Altered drug metabolism and fetal/infant opioid effects
Patients on other predetermined analgesia pathway (for example, regional anaesthesia)	
Previous participation in this study	
Current participation in another clinical trial of an investigational medicinal product	

ED=emergency department; PCA=patient controlled analgesia.

12 hour period. Participants were also instructed on how to record periods asleep, retrospectively, on the booklet by using a tick box on each page.

Most other outcome data were collected for 12 hours from the point at which the first study pain score was completed. Opioid use was recorded from the prescribed drugs administered as recorded on the patient's drug chart during the study period (including that prescribed pre-admission). We used study observation charts, based on standard hospital charts, for all study participants; these were completed as part of routine care by emergency department nurses and then by ward nurses after inpatient admission. Observations followed the standard of care in each centre. Typically, this involved observations hourly for four hours, two hourly for eight hours, and four hourly thereafter. In practice, this meant hourly vital signs in the emergency department and vital signs every two hours for the rest of the study period. Observations included heart rate, blood pressure, respiratory rate, oxygen saturations, oxygen flow rate, sedation score, and nausea score (0-2). A research nurse reviewed the observation charts after the 12 hour study period and transcribed out of range results into the study case report form.

Where possible, at the end of the 12 hour study period (or the following morning as appropriate), a research nurse visited participants in both groups to facilitate data collection. The final page of the data collection booklet included a five point pain management satisfaction score ranging from "perfectly satisfied" to "not satisfied at all." After the participant's discharge, the research nurse obtained the length of stay in hospital and final diagnosis at discharge from the patient administration system (or equivalent) and recorded them in the case report form.

Interventions

Participants allocated to receive routine care were treated with intravenous morphine while in the emergency department and oral morphine (or subcutaneous/intramuscular morphine for those nil by mouth) when transferred to the hospital ward. Participants randomised to the PCA group received instruction from the research nurse in how to operate the PCA device, which was set up by the emergency department nurses and started with a 1 mg morphine bolus and a five minute lockout. PCA was continued for a minimum period of 12 hours; in practice, the clinical team reviewed ongoing requirement for PCA the following morning. Participants in both groups were prescribed multimodal analgesia in addition, including paracetamol and a non-steroidal anti-inflammatory drug (unless contraindicated) and were also prescribed antiemetics as required.

Primary outcome measure

The primary outcome measure was the total pain experienced over the 12 hour study period, as captured by the hourly completion of a visual analogue pain rating scale. We derived this by plotting data as a graph of visual analogue scale pain against time and calculating the area under the curve for each participant. This is a measure of overall pain experienced during the study period.[22]

Secondary outcome measures

Secondary outcome measures included total opioid dose, opioid side effects, patients satisfaction with pain management, proportion of study period in moderate/severe pain (that is, with visual analogue scale >44 mm), proportion of study period spent sleeping, and length of hospital stay.

Randomisation, allocation concealment, and blinding

Randomisation (one to one) to either PCA or routine care was done via a secure web based randomisation system. Research team members accessing the randomisation

website did not know the allocation for an individual patient until the relevant details were entered and recruitment confirmed.

As pain experienced over subsequent hours may be affected by the time of day of recruitment (participants included later in the day would score their pain during night hours when they may spend a greater proportion of time asleep), randomisation was stratified by the time of the first recorded pain score (morning or afternoon/evening), as well as by recruitment centre. Blinding was not possible for this study owing to the nature of the intervention.

Sample size

The main objective of this study was to assess the magnitude of any difference in total pain scores between the PCA and routine care groups. Primary outcome data were collected in terms of self reported pain scores over time, with visual analogue scale measurements completed hourly over the 12 hour study period. We plotted data as a graph of visual analogue scale pain against time and used this to produce an area under the curve for each patient. This is a measure of overall pain experienced during the study period.[22]

Very few studies have considered the question of what reduction in area under the curve might be a clinically significant analgesic effect. One study by Camu et al showed that a 20% reduction in the area under the curve for pain on movement was associated with a 26% absolute increase in the proportion of patients reporting their global rating of pain relief as very good or excellent (P=0.01).[23] Conservatively, therefore, we chose a difference in area under the curve of 15% between PCA and routine care groups to be of clinical significance. On a standardised area under the curve (scoring between 0 and 100), we expected the routine care group to have an average score of about 40 units, so 15% equates to a six point reduction. A standard deviation can be estimated from the research by Camu et al as about 15 units. On the basis of these assumptions, and using a two tailed two sample *t* test, with a type 1 error rate of 0.05, a sample size of 100 participants per group provides sufficient power (80%) to detect a between group difference of 15%.

Statistical analyses

We report and present data according to the relevant CONSORT statement.[24] The primary analyses were all pre-specified in a detailed statistical analysis plan approved by the Data Monitoring Committee before the analyses began. They followed an intention to treat approach, with the intent to treat population defined as all participants who completed the baseline and at least one subsequent pain visual analogue scale. Primary analyses were adjusted for the stratification factors (centre and time of baseline pain score (morning or afternoon/evening)) as fixed effects; unadjusted analyses are also presented. We present 95% confidence intervals for between group differences, with the significance level for hypothesis testing set at 5%.

We captured the primary outcome measure of total pain experienced by using the area under the curve approach and compared it between PCA and routine care groups by using analysis of covariance, including the two stratification variables and the baseline pain score as covariates. This analysis was done blinded to the allocated group. We used the "trapezoidal" rule to calculate the area under the curve, using straight lines to join visual analogue scale scores and calculating the area under them for the 12 hour period. In general, where one or more hourly scores were not recorded, we imputed values by linear interpolation if scores were recorded either side and by last observation carried forward if scores were missing at the end of the 12 hour period, except that we recorded such final scores as zero if the patient was discharged (or self discharged). The Trial Steering Committee and Data Monitoring Committee agreed these conventions in a detailed strategy, and reasons for missing data were categorised by a member of the Trial Management Group blinded to participants' allocated group wherever possible.

We similarly compared continuous secondary outcomes between the two groups by using analysis of covariance, with adjustment for the two stratification variables. Given that some visual suggestion of potential violations of the linear model assumptions existed, we also produced bootstrapped confidence intervals for the between group differences for each outcome measure. In each instance, little difference existed between the normal based and bootstrapped confidence intervals; for simplicity, we present only the normal based confidence intervals.

For the analysis of participants' satisfaction with pain management, we recoded the five point scale (ranging from "perfectly satisfied" to "not at all satisfied") into two categories, combining "perfectly satisfied" and "very satisfied" into one category and the others into a second category. We used binary logistic regression to determine the odds ratio and 95% confidence interval for the group effect, with adjustment for the stratification variables. Similar analyses compared the proportions of participants in terms of side effects.

Sensitivity analyses

We did two pre-specified sensitivity analyses of the primary outcome measure: the first scored pain as zero for periods of sleep (sensitivity 1) and the second imputed missing pain scores due to transfers to theatre by using linear interpolation from the last recorded pain score to zero at the 12 hour time point (sensitivity 2).

Patient involvement

During the design of this study, a patient representative contributed to the development of the grant application and, later, to the study protocol and participant facing documentation after funding had been awarded. We also had a patient representative on the Trial Steering

Committee who helped to oversee progress of the trial and provided a patient's perspective on aspects of trial conduct. A lay summary of the study findings will be made available to participants at www.medicalresearchplymouth.org.uk.

Results

Recruitment and flow through trial

The figure outlines the flow of participants in the trial. Recruitment took place from July 2011 to November 2013. Of 319 eligible patients who were approached to participate, 59 (18%) declined and a further 39 (12%) did not participate for other reasons. The remaining 221 patients consented and were randomised: 108 to PCA and 113 to treatment as usual. Seven participants in the PCA group and 10 participants in the treatment as usual group were not included in the statistical analyses, predominately owing either to the booklets with the pain scores going missing or to the partici-

pant completing the pain score only once. One participating hospital experienced some local difficulties in implementing the protocol as intended and only four patients were recruited at this site, making the pre-specified adjustment for centre impossible. On the advice of the Data Monitoring Committee, we excluded data from this site from the primary analyses, and the two participants in each group were replaced with newly recruited participants from other sites. Thus the primary analyses are based on 200 participants, 99 randomised to PCA and 101 randomised to treatment as usual.

Baseline characteristics

Participants were aged 18 to 75 years, and 142 (71%) were men (table 2). At the time of admission to the emergency department, participants' median verbal rated pain score was 7.0 (range 0-10). The median time from arrival in the emergency department to randomisation was 137 (range 17-385) minutes. By the time participants completed their first study pain score, the median visual analogue pain score overall was 5.3 (range 0.1-10). The two randomised groups were similar in terms of most characteristics.

Primary outcome (including sensitivity analyses)

Mean total pain experienced in the PCA group was 44.0 (SD 24.0) compared with 47.2 (21.9) in the treatment as usual group (table 3). The primary analysis, with adjustment for centre, time of baseline pain score, and baseline pain score, indicated slightly (but not statistically significantly) lower mean total pain experienced in the PCA group than in the routine care group (mean difference 2.7, 95% confidence interval −2.4 to 7.8). In both pre-specified sensitivity analyses, the between group difference was of a similar magnitude.

Secondary outcomes

Participants allocated to PCA used significantly more morphine in total than did participants in the treatment as usual group (mean 44.3 (SD 23.2) v 27.2 (18.2) mg; adjusted mean difference 17.0 (11.3 to 22.7) mg) (table 4). Participants in the PCA group also used significantly more morphine during the 12 hour study period (adjusted mean difference 15.8 (11.2 to 20.5) mg).

PCA participants spent, on average, less time in moderate/severe pain (mean 36.2% (SD 31.0) v 44.1% (31.6)), but the difference was not statistically significant. We found no evidence of differences between the groups in terms of the percentage of the study period spent asleep or the length of hospital stay. Although a higher proportion of PCA participants reported being perfectly or very satisfied compared with the treatment as usual group (78/91 (86%) v 74/98 (76%)), this did not reach statistical significance (adjusted odds ratio 1.91, 95% confidence interval 0.90 to 4.07).

A higher proportion of the PCA group experienced at least one out of range vital signs measurement compared with the treatment as usual group (29/99 (29%) v 21/101 (21%)). In particular, a significantly greater
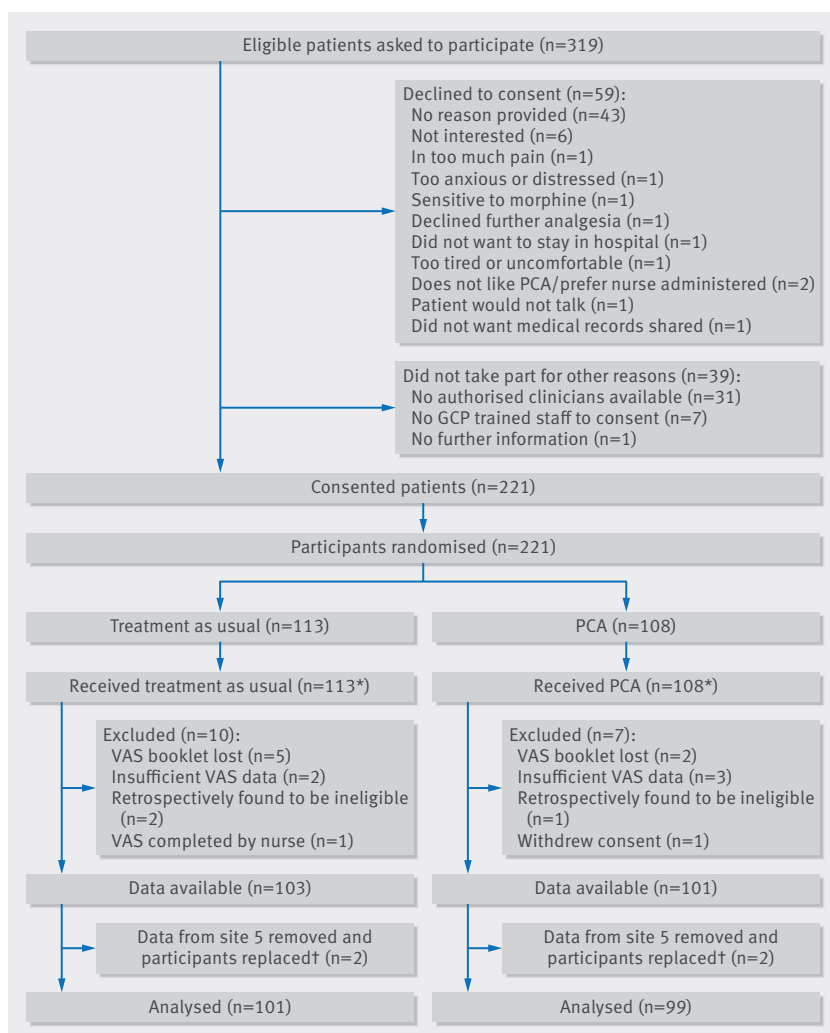
Flow of participants through study. GCP=good clinical practice; PCA=patient controlled analgesia; VAS=visual analogue scale. *8 participants transferred between treatment groups during 12 hour study period: 2 patients discontinued PCA and went into treatment as usual; 6 went the other way. †Following advice from the Data Monitoring Committee's independent statistician, participants recruited at site 5 were excluded and replaced with newly recruited participants from other sites

Table 2 | Baseline and demographic data. Values are percentages (numbers) unless stated otherwise

	Patient controlled analgesia (n=99)	Treatment as usual (n=101)	All (n=200)
Demographics			
Male sex	74 (73)	68 (69)	71 (142)
Mean (SD; range) age, years	43.6 (15.1; 18-74)	42.5 (14.8; 18-75)	43.1 (15.0; 18-75)
Median (IQR; range) verbal rated pain score (0-10, as recorded on hospital administration system)	7 (5-8; 0-10) (n=88)	7 (5-8; 0-10) (n=96)	7 (5-8; 0-10) (n=184)
Median (IQR; range) visual analogue pain score (at time of consent), cm	4.8 (2.9-7.3; 0.1-10)	5.4 (3.8-7.2; 0.1-9.7)	5.3 (3.1-7.3; 0.1-10)
Time of recruitment			
Morning (0600-1159)	16 (16)	16 (16)	16 (32)
Afternoon (1200-2200)	84 (83)	84 (85)	84 (168)
Median (IQR; range) time from arrival in emergency department to randomisation	144 (101-197; 24-385)	132 (93-182; 17-332)	137 (98-189.5; 17-385)
Recruitment centre			
Centre 1	36 (36)	35 (35)	36 (71)
Centre 2	9 (9)	9 (9)	9 (18)
Centre 3	5 (5)	5 (5)	5 (10)
Centre 4	49 (49)	51 (52)	51 (101)
Clinical diagnosis*			
Burns	0 (0)	2 (2)	1 (2)
Chest wall injury	10 (10)	12 (12)	11 (22)
Lower limb fracture	28 (28)	34 (34)	31 (62)
Multiple injuries	30 (30)	22 (22)	26 (52)
Pelvis fracture	11 (11)	7 (7)	9 (18)
Spine fracture	6 (6)	10 (10)	8 (16)
Upper limb fracture	6 (6)	5 (5)	6 (11)
Soft tissue injury	6 (6)	8 (8)	7 (14)
Other	2 (2)	1 (1)	2 (3)
Preadmission analgesia			
Mean (SD; range) morphine (mg):			
Participants with pre-admission morphine	10.3 (6.7; 1.7-40.0) (n=64)	10.5 (6.0; 1.0-30.0) (n=65)	10.4 (6.3; 1.0-40.0) (n=129)
All participants	6.7 (7.3; 0-40.0)	6.8 (7.0; 0-30.0)	6.7 (7.1; 0-40.0)
At least one dose in 24 hours before emergency department arrival:			
Analgesic gas	7 (7)	7 (7)	7 (14)
Non-steroidal anti-inflammatory drug	1 (1)	2 (2)	2 (3)
Paracetamol	15 (15)	14 (14)	15 (29)
Weak opioid	6 (6)	2 (2)	4 (8)
Adjuvant weak opioid	7 (7)	5 (5)	6 (12)

*Taken from participants' discharge summaries.

Table 3 | Primary outcome of total pain experienced (standardised area under curve): primary and sensitivity analyses

	Mean (SD; range)		Adjusted analysis*		Unadjusted analysis	
Analysis	Treatment as usual (n=101)	Patient controlled analgesia (n=99)	Mean difference† (95% CI)	P value	Mean difference† (95% CI)	P value
Primary	47.2 (21.9; 6.4-96.2)	44.0 (24.0; 1.0-96.8)	2.7 (−2.4 to 7.8)	0.290	3.2 (−3.2 to 9.7)	0.321
Sensitivity 1‡	36.7 (20.9; 2.5-96.2)	32.3 (20.0; 1.0-93.3)	4.0 (−0.8 to 8.8)	0.101	4.4 (−1.3 to 10.1)	0.127
Sensitivity 2§	46.5 (21.2; 6.4-96.2)	43.7 (24.2; 0.9-96.8)	2.3 (−2.8 to 7.4)	0.374	2.8 (−3.6 to 9.1)	0.389

*Adjusted for stratification variables (time of first pain score and recruitment centre) and baseline pain score.
†Treatment as usual minus patient controlled analgesia.
‡Pain scored as zero for periods of sleep.
§Missing pain scores for theatre withdrawals imputed using linear interpolation from last recorded pain score to zero at 12 hour time point.

proportion of participants in the PCA group experienced one or more episodes of nausea (adjusted odds ratio 5.98, 1.23 to 29.04). One participant in the PCA group also had one instance of hypoxia.

Adverse events

One serious adverse event was reported during the study for a participant allocated to the PCA group.

The event was summarised as drowsiness probably related to opiates; the patient recovered fully. Four non-serious adverse effects were reported. Three were mild in severity, all related to morphine and expected (itching). One non-serious adverse event was moderate in severity and reported as drowsiness and vomiting; this was considered related to morphine and was expected.

Table 4 | Secondary outcomes

Outcome	Mean (SD; range)		Adjusted analysis*		Unadjusted analysis	
	TAU (n=101)	PCA (n=99)	Mean difference† (95% CI)	P value	Mean difference† (95% CI)	P value
Total morphine (mg)‡	27.2 (18.2; 3.3-92.3)	44.3 (23.2; 5.0-128.0)	−17.0 (−22.7 to −11.3)	<0.001	−17.1 (−22.9 to −11.3)	<0.001
Total morphine during 12 hour study period (mg)	12.3 (14.2; 0-82.3)	28.1 (19.4; 0-103.0)	−15.8 (−20.5 to −11.2)	<0.001	−15.8 (−20.5 to −11.0)	<0.001
Percentage of study period with pain VAS >44 mm	44.1 (31.6; 0-100)	36.2 (31.0; 0-100)	7.8 (−1.0 to 16.5)	0.081	7.9 (−0.8 to 16.6)	0.075
Percentage of study period asleep	22.6 (20.5; 0-76.9)	24.9 (21.2; 0-76.9)	−2.3 (−8.2 to 3.5)	0.432	−2.3 (−8.2 to 3.5)	0.430
Length of hospital stay (days)	7.0 (7.8; 0.2-56.1)	9.2 (11.4; 0.3-71.9)	−2.3 (−4.9 to 0.4)	0.097	−2.2 (−4.9 to 0.5)	0.112

PCA=patient controlled analgesia; TAU=treatment as usual; VAS=visual analogue scale.
*Adjusted for stratification variables (time of first pain score and recruitment centre).
†TAU minus PCA.
‡Sum of pre-admission morphine, morphine from time of admission to time of recruitment, and morphine delivered during 12 hour study period.

Discussion

This study found no statistically significant difference in effectiveness between PCA and treatment as usual in emergency patients admitted to hospital with pain from traumatic injuries. Although we saw a modest reduction in overall pain scores and a reduction in the amount of time that patients spent in moderate and severe pain, neither of these reached statistical significance. Moreover, the point estimate of the effect of the primary outcome was lower than our presumed threshold for clinical importance (that is, six points). However, as our confidence interval for the difference between groups included this difference of six points, we cannot rule out the possibility that PCA provides a clinical benefit. Significantly more morphine was used in the PCA group, which may reflect under-treatment in the routine care group. Patients' satisfaction also showed a difference in favour of PCA; the difference did not reach statistical significance, although it may be clinically important.

Strengths and limitations of study

The main strength of this study was that it combined care in the emergency department with ongoing care once the patient was admitted to a hospital ward. It investigated the effects of PCA started in the emergency department but also subsequently beyond the patient's emergency department stay. This is the first study to look at this vulnerable period between emergency care and inpatient management.

The lack of blinding in this study could be viewed as a limitation, but we did not consider blinding of patients or clinicians to the treatment allocation practical. The potential variability in usual treatment between hospitals could also be viewed as a limitation.

We emphasise that the routine care arm of this study may not represent real world emergency care. All patients who were allocated to the routine care group were prescribed multimodal analgesia according to the hospital guideline, but in many cases and for a variety of reasons this may not always occur in normal practice. There may also have been a Hawthorne effect on the nurses who were looking after the patients in the routine care group; they knew that they were being observed, so their review of the patients' analgesic requirements may have been influenced by this.

Comparisons with other studies and implications of study

Before this study started, only one small randomised trial of 86 adult patients with pain due to trauma presenting to a UK emergency department had been published,[17] which concluded that PCA was as effective as standard nurse titrated analgesia. However, the trial collected data during the patients' emergency department stay only and did not continue to follow them after admission to a hospital ward. Three further relevant studies have been reported since this study started, although all three were limited to a two hour period in the emergency department. The largest,[18] a study done in North America, randomised 211 emergency patients with abdominal pain to one of three groups: standard care, PCA standard dose (1 mg) bolus, or PCA higher dose (1.5 mg) bolus. It found a significant reduction in pain in both PCA groups compared with standard care. A smaller study from Malaysia included patients presenting with pain of traumatic origin[19]; 96 patients in two centres were randomised to either standard care or PCA (1 mg boluses), with a significant reduction reported in pain scores in the PCA group compared with the standard care group. The same two authors reported another smaller study of 47 patients with traumatic injury.[20] Patients were again randomised to receive either standard care or PCA (1 mg boluses). This study found similar reductions in pain scores in the PCA group compared with standard care.

Conclusions

This study has shown that for patients with traumatic injuries, PCA had no statistically significant benefit over standardised routine care. This is the first study to follow up participants from emergency admission to the hospital ward, and it has therefore given a pragmatic answer to the question of whether PCA should be used in these patients.

1 Merskey H. Pain terms: a list with definitions and notes on usage. Recommended by the IASP Subcommittee on Taxonomy. Pain 1979;6:249.
2 Todd KH, Ducharme J, Choiniere M, et al. Pain in the emergency department: results of the pain and emergency medicine initiative (PEMI) multicenter study. J Pain 2007;8:460-6.
3 Care Quality Commission. Accident and emergency 2012. http://webarchive.nationalarchives.gov.uk/20121213135835/http://www.cqc.org.uk/public/reports-surveys-and-reviews/surveys/accident-and-emergency-2012.
4 College of Emergency Medicine. Clinical standards for emergency departments. 2014. www.rcem.ac.uk/Shop-Floor/Clinical%20Standards.
5 Plummer JL, Owen H, Ilsley AH, et al. Morphine patient-controlled analgesia is superior to meperidine patient-controlled analgesia for postoperative pain. Anesth Analg 1997;84:794-9.
6 Lvovschi V, Aubrun F, Bonnet P, et al. Intravenous morphine titration to treat severe pain in the ED. Am J Emerg Med 2008;26:676-82.
7 Arendts G, Fry M. Factors associated with delay to opiate analgesia in emergency departments. J Pain 2006;7:682-6.
8 Owen H, Plummer JL, Armstrong I, et al. Variables of patient-controlled analgesia: 1. Bolus size. Anaesthesia 1989;44:7-10.
9 Owen H, Szekely SM, Plummer JL, et al. Variables of patient-controlled analgesia: 2. Concurrent infusion. Anaesthesia 1989;44:11-3.
10 Macintyre PE. Safety and efficacy of patient-controlled analgesia. Br J Anaesth 2001;87:36-46.
11 Walder B, Schafer M, Henzi I, et al. Efficacy and safety of patient-controlled opioid analgesia for acute postoperative pain: a quantitative systematic review. Acta Anaesthesiol Scand 2001;45:795-804.
12 Choiniere M, Grenier R, Paquette C. Patient-controlled analgesia: a double-blind study in burn patients. Anaesthesia 1992;47:467-72.
13 Hudcova J, McNicol E, Quah C, et al. Patient controlled opioid analgesia versus conventional opioid analgesia for postoperative pain. Cochrane Database Syst Rev 2006;4:CD003348.
14 White PF. Use of patient-controlled analgesia for management of acute pain. JAMA 1988;259:243-7.
15 Dolin SJ, Cashman JN, Bland JM. Effectiveness of acute postoperative pain management: I. Evidence from published data. Br J Anaesth 2002;89:409-23.
16 Rees DC, Olujohungbe AD, Parker NE, et al. Guidelines for the management of the acute painful crisis in sickle cell disease. Br J Haematol 2003;120:744-52.
17 Evans E, Turley N, Robinson N, et al. Randomised controlled trial of patient controlled analgesia compared with nurse delivered analgesia in an emergency department. Emerg Med J 2005;22:25-9.
18 Birnbaum A, Schechter C, Tufaro V, et al. Efficacy of patient-controlled analgesia for patients with acute abdominal pain in the emergency department: a randomized trial. Acad Emerg Med 2012;19:370-7.
19 Rahman NH, DeSilva T. A randomized controlled trial of patient-controlled analgesia compared with boluses of analgesia for the control of acute traumatic pain in the emergency department. J Emerg Med 2012;43:951-7.
20 Rahman NH, DeSilva T. The effectiveness of patient control analgesia in the treatment of acute traumatic pain in the emergency department: a randomized controlled trial. Eur J Emerg Med 2012;19:241-5.
21 Smith JE, Rockett M, Squire R, et al. PAin SoluTions In the Emergency Setting (PASTIES); a protocol for two open-label randomised trials of patient-controlled analgesia (PCA) versus routine care in the emergency department. BMJ Open 2013;3:pii:e002577.
22 Matthews JN, Altman DG, Campbell MJ, et al. Analysis of serial measurements in medical research. BMJ 1990;300:230-5.
23 Camu F, Van Aken H, Bovill JG. Postoperative analgesic effects of three demand-dose sizes of fentanyl administered by patient-controlled analgesia. Anesth Analg 1998;87:890-5.
24 Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. BMJ 2010;340:c869.