The impact of emergency department patient-controlled analgesia (PCA) on the incidence of chronic pain following trauma and non-traumatic abdominal pain*

M. Rockett, S. Creanor, R. Squire, A. Barton, J. Benger, L. Cocking, P. Ewings, V. Eyre and J. E. Smith

1 Consultant in Anaesthesia and Pain Medicine, 3 Lead research nurse, 9 Consultant in Emergency Medicine, Plymouth University Hospitals NHS Trust, Plymouth, UK
2 Associate Professor in Clinical Trials and Medical Statistics, 6 Senior data manager, University of Plymouth, Plymouth, UK
4 Consultant, 7 Director, NIHR Research Design Service South West, UK
5 Professor of Emergency Care, Faculty of Health and Applied Sciences, University of the West of England, Bristol, UK
8 UK Clinical Trials Operations Manager, Re:Cognition Health Ltd, Plymouth, UK

Summary
The effect of patient-controlled analgesia during the emergency phase of care on the prevalence of persistent pain is unknown. We studied individuals with traumatic injuries or abdominal pain 6 months after hospital admission via the emergency department using an opportunistic observational study design. This was conducted using postal questionnaires that were sent to participants recruited to the multi-centre pain solutions in the emergency setting study. Patients with prior chronic pain states or opioid use were not studied. Questionnaires included the EQ5D, the Brief Pain Inventory and the Hospital Anxiety and Depression scale. Overall, 141 out of 286 (49% 95%CI 44–56%) patients were included in this follow-up study. Participants presenting with trauma were more likely to develop persistent pain than those presenting with abdominal pain, 45 out of 64 (70%) vs. 24 out of 77 (31%); 95%CI 24–54%, p < 0.001. There were no statistically significant associations between persistent pain and analgesic modality during hospital admission, age or sex. Across both abdominal pain and traumatic injury groups, participants with persistent pain had lower EQ5D mobility scores, worse overall health and higher anxiety and depression scores (p < 0.05). In the abdominal pain group, 13 out of 50 (26%) patients using patient-controlled analgesia developed persistent pain vs. 11 out of 27 (41%) of those with usual treatment; 95%CI for difference (control – patient-controlled analgesia) −8 to 39%, p = 0.183. Acute pain scores at the time of hospital admission were higher in participants who developed persistent pain; 95%CI 0.7–23.6, p = 0.039. For traumatic pain, 25 out of 35 (71%) patients given patient-controlled analgesia developed persistent pain vs. 20 out of 29 (69%) patients with usual treatment; 95%CI −30 to 24%, p = 0.830. Persistent pain is common 6 months after hospital admission, particularly following trauma. The study findings suggest that it may be possible to reduce persistent pain (at least in patients with abdominal pain) by delivering better acute pain management. Further research is needed to confirm this hypothesis.

Correspondence to: M. Rockett
Email: mark.rockett@nhs.net
Accepted: 25 September 2018
Keywords: acute pain; patient-controlled analgesia; persistent pain
*Presented in part as a poster at the National Acute Pain Symposium, Chester, UK, September 2014.
Twitter: @mark_rockett

© 2018 The Authors. Anaesthesia published by John Wiley & Sons Ltd on behalf of Association of Anaesthetists.
This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.
Introduction

Pain is the commonest reason for presentation to the emergency department (ED) [1]. Two common diagnostic groups are patients with traumatic injury and non-traumatic abdominal pain. These patients frequently experience severe acute pain that is often managed in the ED with opioid analgesics [2, 3]. Although pain scores usually reduce after discharge from hospital, 21% of individuals experience persistent pain [4]. In the postoperative setting, an adverse ‘pain trajectory’ has been correlated with persistent postoperative pain, and it is reasonable to suspect that this might also predispose to persistent pain in the ED patient population [5]. Persistent pain may be defined as pain continuing beyond the expected time of healing, usually 3–6 months [6].

Persistent pain following surgery is common in the general population [7, 8]. The incidence of significant persistent postoperative pain for all operation types is 11.8% at 1 year [9]. Persistent non-cancer pain is correlated with poor mental health, loss of employment and a poor quality of life [10].

The transition from acute to persistent pain has been less well investigated after trauma or following an episode of acute abdominal pain. Following traumatic injury, persistent pain is common, with 44% of patients reporting accident-related pain 3 years later in one prospective study [11]. Little is known about the development of persistent abdominal pain after the initial presentation. Recurrent or chronic abdominal pain is common in children, occurring in up to one-fifth of individuals [12]. In adults, abdominal and pelvic pain are also frequent. The monthly prevalence and incidence rates of chronic pelvic pain are 21.5/1000 and 1.58/1000, respectively, with an annual prevalence of 38.3/1000 [13].

There are multiple risk factors for the progression from acute to persistent pain [14]. These include: type of injury; surgery or other pathology (nerve injury, tissue trauma and inflammation are all important); and a number of patient-specific factors including: sex; age; genetics; anxiety; depression and abnormal coping responses [11, 15]. The presence of severe acute postoperative pain consistently correlates with the development of persistent postoperative pain [16]. It is possible that improved pain relief in the acute phase following a traumatic injury or during an episode of non-traumatic abdominal pain may reduce the frequency of persistent pain 6 months later.

We have demonstrated that patient-controlled analgesia (PCA) results in improved analgesia in the short term for patients admitted with abdominal pain to hospital via the ED [3]. The impact of PCA on the incidence of persistent pain is unknown. The aim of this study was to determine whether PCA use in the first 12 h of care alters the prevalence of persistent pain 6 months later for this group of patients. Secondary aims were to assess the impact of persistent pain on mental health and quality of life.

This is the first study to investigate the incidence of persistent pain in a population without pre-existing pain or opioid use, and may suggest hypotheses for future research into its prevention after trauma or acute abdominal pain.

Methods

This was an opportunistic observational study. The study sample was drawn from participants enrolled in the pain solutions in the emergency setting study. This comprised two parallel, multi-centre, open-label randomised trials of PCA vs. usual treatment (control) that were statistically powered separately but run side-by-side using a shared protocol. Participants were adults presenting to the ED with either traumatic injury or non-traumatic abdominal pain requiring intravenous opioid analgesia and hospital admission. Exclusion criteria included age > 75 years and a history of other chronic pain conditions or opioid use. Visual analogue pain scores were recorded hourly for the first 12 h, and the ‘total pain experienced’ was calculated as the area under the curve of pain score against time, standardised to a score from 0 to 100 units [17]. Acute pain at the time of hospital admission was measured over 12 h as described above, and quality of life was measured using the EQ5D. Anxiety and depression were assessed using the hospital anxiety and depression scale (HADS). Scores of ≥ 8/21 on either the anxiety or depression subscale of the HADS were clinically significant.

Questionnaire booklets were sent to study participants recruited at three centres 6 months after admission to hospital. If no reply was received within 2 weeks, a second questionnaire pack was sent. If no reply was received to the second questionnaire pack, the participants were contacted by telephone and a third pack was sent.

The primary outcome measure was the presence of pain at 6 months. This was defined as a positive answer to the question: ‘Do you continue to experience pain which you attribute to the injury or episode of abdominal pain you experienced approximately 6 months ago, when you attended the Emergency Department?’ Persistent pain was assessed using the Brief Pain Inventory (BPI). Significant persistent pain was defined as average pain ≥ 4 or worst pain ≥ 8.
The proportion of participants with significant persistent pain at 6 months was calculated and compared between randomised groups (control or PCA, on intention-to-treat basis), overall and separately for each group (abdominal pain or trauma), using tests of proportions at the 5% significance level and corresponding 95%CI. As this was an exploratory follow-up study, no adjustments were made for multiple testing.

The hypothesis was that use of PCA to manage an episode of acute non-traumatic abdominal pain or pain from traumatic injury would result in a reduction in the risk of significant persistent pain 6 months later. Secondary aims were to assess the impact of acute pain on the prevalence of significant persistent pain at 6 months. We also assessed the impact of persistent pain on quality of life measures, and compared the levels of anxiety and depression in patients with and without significant persistent pain following an acute pain episode.

Results

The response rate was 141/286 (49%); 95%CI 43–55% (Table 1), and the diagnostic categories of participants are listed in Table 2. Almost half of the respondents continued to experience pain 6 months after the index event (69 out of 141 (49%); 95%CI 40–58%). The proportion of participants experiencing persistent pain differed between the two groups, with 24 out of 77 (31%) patients in the non-traumatic abdominal pain group and 45 out of 64 (70%) patients in the traumatic injury pain group affected. The difference in the prevalence of significant persistent pain at 6 months between the two groups was statistically significant; 95%CI for difference (trauma – abdominal related pain) 24–54%, p < 0.001, and they were therefore analysed separately.

If it is conservatively assumed that participants who did not return their questionnaire did not have significant pain at 6 months, then the estimated prevalence of significant persistent pain is 24 out of 180 (13%) and 45 out of 99 (46%) patients for the abdominal pain group and traumatic injury pain group, respectively.

At 6 months, 54 out of 77 (70%) participants were pain free, 11 out of 77 (14%) had mild pain and 12 out of 77 (16%) had significant pain. Eleven out of 27 (41%) of those allocated to the control group reported persistent pain vs. 13 out of 50 (26%) of those allocated to PCA. This difference was not statistically significant; 95%CI for difference (control – PCA) −8 to 39%, p = 0.183. The association between persistent pain and sex was not statistically significant, with 5 out of 27 (19%) men reporting persistent pain at 6 months compared with 19 out of 50 (38%) women; 95%CI for difference (females – males) 0–42%, p = 0.078. Those with persistent abdominal pain at 6 months had experienced statistically significant higher standardised pain scores in the first 12 h of the PASTIES study; mean difference 12.1 units (persistent pain – no persistent pain); 95%CI for difference 0.7 – 23.6, p = 0.039.

Data from the EQ5D questionnaire revealed a marked impact on mobility. Nine out of 24 (38%) participants with persistent pain stated they had reduced mobility vs. 4 out of 52 (8%) of those without ongoing pain; 95%CI for difference (persistent pain – no persistent pain) 18–73%, p = 0.003. General health state was also worse with persistent pain.

| Table 1 | Recruitment from Plymouth, Bristol and Exeter centres. |
|---------|-------------------------------------------------------|
| Participants recruited to primary study [17] | 294 |
| Participants not included in this study | 8 |
| Participants contacted | 286 |
| Usable questionnaires returned | 141 |
| Total questionnaires sent | 492 |
| Returned after initial post | 85 |
| Returned after first chase | 59 |
| Total phone calls made | 57 |
| Returned after phone calls | 0 |

©2018 The Authors. Anaesthesia published by John Wiley & Sons Ltd on behalf of Association of Anaesthetists.
mean difference –12.9 units (persistent pain – no persistent pain); 95%CI –24.5 to –1.4, p = 0.029. There were significantly higher anxiety and depression scores in the group with persistent abdominal pain than the group without persistent pain, mean difference 3.2 units (persistent pain – no persistent pain); 95%CI 1.2 – 5.2, p = 0.003, depression 3.3 units (mean difference); 95%CI 1.1–5.5, p = 0.005. See Fig. 1.

At 6-month follow-up, 19 out of 64 (30%) participants were pain free, 30 out of 64 (47%) had mild pain and 15 out of 64 (23%) had significant persistent pain. Use of PCA in the first 12 h had little effect on the occurrence of persistent pain at 6 months in this group. Twenty out of 29 (69%) patients allocated to the control group reported ongoing pain at 6 months, compared with 25 out of 35 (71%) allocated to PCA; 95%CI for difference (control – PCA) –30 to 24%, p = 0.830. The association between sex and persistent pain in the trauma group was not statistically significant, with 29 out of 37 (78%) men reporting continuing pain at 6 months compared with 16 out of 27 (59%) women; 95%CI for difference (females – males) –46 to 4%, p = 0.098. In the trauma group there was no association between standardised pain scores in the first 12 h and persistent pain at 6 months, mean difference 0.6 units (persistent pain – no persistent pain); 95%CI −13.7 to 14.9, p = 0.936.

The impact of persistent pain after trauma was noteworthy. Mobility was impaired for 28 out of 44 (64%) participants with persistent pain vs. 3 out of 19 (16%) for those without persistent pain; 95%CI for difference (persistent pain – no persistent pain); 20–61%, p = 0.008. The proportion of participants reporting moderate pain or discomfort on EQ5D was 35 out of 43 (81%) among participants with persistent pain vs. 10/19 (53%) for those without persistent pain; 95%CI for difference (persistent pain – no persistent pain) 4–57%, p = 0.030. General health was also worse with persistent pain, mean difference of –15.8 units (persistent pain – no persistent pain); 95%CI –22.7 to –8.9, p < 0.001. There were significantly higher anxiety and depression scores in the group with persistent abdominal pain than the group without. Anxiety: mean difference 2.7 units (persistent pain – no persistent pain); 95%CI 0.7–4.8, p = 0.010; depression mean difference 2.7 units; 95%CI 0.9–4.4, p = 0.004 (see Fig. 1).

**Discussion**

This study has demonstrated the significant burden of persistent pain following admission to hospital with pain due to traumatic injuries or non-traumatic abdominal pain. This is the first study designed to investigate the incidence of persistent pain in an ED patient population without pre-existing pain problems, and to characterise that pain and impact on well-being.

The response rate was 49% by the end of data collection. Sixty percent of the useable questionnaires were received after the first posting and 40% after the second. Telephone calls and a third posting did not result in any further useable questionnaires. Three questionnaires were unusable. There may have been a response bias, as it might be expected that participants without pain after a brief hospital visit 6 months earlier would be less likely to return their follow-up questionnaires. All participants in this study had successfully completed the questionnaires included in the acute pain study.

Following an episode of acute abdominal pain, persistent pain was common. For this group, there was no statistically significant sex difference in the prevalence of persistent pain, with 38% of women and 19% of men affected. Anxiety and depression were higher in patients with persistent pain, and overall health status was poorer. Mobility was significantly impaired by persistent abdominal pain. Participants with persistent pain had experienced significantly higher standardised acute pain scores in the first 12 h. Fewer patients experienced persistent pain if treated with a PCA, although it was not statistically significant in this opportunistic sample (26% in the PCA group vs. 41% in the control group). These findings are perhaps not surprising, as severe acute pain is known to be a predictor of persistent pain in the surgical setting, and the our previous study demonstrated that PCA use resulted in better analgesia in the abdominal pain group[3].

A different picture was observed in participants with acute pain from traumatic injuries. The prevalence of persistent pain in this group was significantly higher than in
the non-traumatic abdominal pain group. Acute pain scores did not differ from patients with non-traumatic abdominal pain, but persistent pain was a more common outcome in the trauma pain group. The severity of acute pain or the use of PCA did not correlate with the presence of persistent pain for the traumatic pain group. The impact of persistent pain was marked, with lower quality of life scores, higher rates of anxiety and depression and interference with mobility.

Persistent pain is common following ED admission with acute pain in those with no prior history of pain problems, analgesia use or mental health problems. Substantial numbers of individuals will be affected by significant persistent pain, resulting in a low quality of life and high rates of psychological illness. For the non-traumatic abdominal pain group, it is imperative to manage acute pain effectively to reduce the incidence of persistent pain and disability. This study was not powered to detect a difference in persistent pain prevalence with PCA use, but the results permit an appropriately powered study to be designed. PCA use costs an additional £20.18 (€22.63 US$26.45) per 12 h in patients with abdominal pain [18]. If PCA reduces the prevalence of persistent pain following acute abdominal pain, it would be the first effective and cost-effective intervention discovered to date.

Participants presenting with pain due to traumatic injuries frequently suffer persistent pain, but there appears to be a lack of correlation between the severity of acute pain and persistent pain prevalence in this group. This finding warrants further study.

Acknowledgements
This study was funded by the NIAA Wiley-Blackwell Anaesthesia Research Grant Number WKRO-2011-0073. In addition to the authors, the manuscript-writing group included C Hayward (Quality Assurance Manager, University of Plymouth) and C Pritchard (Consultant, NIHR Research Design Service South West).

References
1. Todd KH, Ducharme J, Todd KH, et al. Pain in the emergency department: results of the pain and emergency medicine initiative (PEMI) multicenter study. Journal of Pain 2007; 8: 460–6.
2. Smith JE, Rockett M, Creanor S, et al. Pain Solutions in the Emergency Setting (PASTIES)-patient controlled analgesia versus routine care in emergency department patients with pain from traumatic injuries: randomised trial. British Medical Journal 2015; 350: h2988.
3. Smith JE, Rockett M, Creanor S, et al. Pain Solutions in the Emergency Setting (PASTIES)-patient controlled analgesia versus routine care in emergency department patients with non-traumatic abdominal pain: randomised trial. British Medical Journal 2015; 350: h3147.
4. Chapman CR, Fosnocht D, Donaldson GW. Resolution of acute pain following discharge from the emergency department: the acute pain trajectory. Journal of Pain 2012; 13: 235–41.
5. Althaus A, Arranz Becker O, Neugebauer E. Distinguishing between pain intensity and pain resolution: using acute post-surgical pain trajectories to predict chronic post-surgical pain. European Journal of Pain 2014; 18: 513–21.
6. Werner MU, Kongsgaard UE. Defining persistent post-surgical pain: is an update required? British Journal of Anaesthesia 2014; 113: 1–4.
7. Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. European Journal of Pain 2006; 10: 287–333.
8. Crombie IK, Davies HT, Macrae WA. Cut and thrust: antecedent surgery and trauma among patients attending a chronic pain clinic. Pain 1998; 76: 167–71.
9. Fletcher D, Stamer UM, Pogatzki-Zahn E, et al. Chronic postsurgical pain in Europe: an observational study. European Journal of Anaesthesiology 2015; 32: 725–34.
10. Fine PG. Long-term consequences of chronic pain: mounting evidence for pain as a neurological disease and parallels with other chronic disease states. Pain Medicine 2011; 12: 996–1004.
11. Jenewein JMoergeli H, Wittmann L, Buchi S, Kraemer B, Schnyder U. Development of chronic pain following severe accidental injury. Results of a 3-year follow-up study. Journal of Psychosomatic Research 2009; 66: 119–26.
12. Hyman PE. Chronic and recurrent abdominal pain. Pediatric Review 2016; 37: 377–90.
13. Zondervan KT, Yudkin PL, Vessey MP, Dawes MG, Barlow DH, Kennedy SH. Prevalence and incidence of chronic pelvic pain in primary care: evidence from a national general practice database. British Journal of Obstetrics and Gynaecology 1999; 106: 1149–55.
14. McGreevy K, Bottros MM, Raja SN. Preventing chronic pain following acute pain: risk factors, preventive strategies, and their efficacy. European Journal of Pain Supplements 2011; 5: 365–72.
15. Lavand’homme P. The progression from acute to chronic pain. Current Opinion in Anaesthesiology 2011; 24: 545–50.
16. Althaus A, Hinrichs-Rocker A, Chapman R, et al. Development of a risk index for the prediction of chronic post-surgical pain. European Journal of Pain 2012; 16: 901–10.
17. Smith JE, Rockett M, Creanor S, 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. British Medical Journal Open 2013; 3: e002577.
18. Pritchard C, Smith JE, Creanor S, et al. The cost-effectiveness of patient-controlled analgesia vs. standard care in patients presenting to the Emergency Department in pain, who are subsequently admitted to hospital. Anaesthesia 2017; 72: 935–9.