Opioid and non-opioid pain relief after an emergency department acute pain visit

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Abstract

Objectives Treatment of acute pain after emergency department (ED) discharge remains a challenge in the opioid crisis context. Our objective was to determine the proportion of patients using opioid vs non-opioid pain medication following discharge from the ED with acute pain, and the association of type of pain medication with average pain intensity before pain medication intake and report of pain relief.

Methods This was a prospective cohort study of ED patients aged ≥ 18 years with an acute pain (≤ 2 weeks) who were discharged with an opioid prescription. Patients completed a 14-day diary assessing daily pain intensity level before each pain medication intake (0–10 numeric rating scale), type of pain medication use (opioid vs non-opioid), and if pain was relieved by the medication used that day. Multilevel analyses were used to compare the effect of type of analgesic used on pain intensity and relief.

Results A total of 381 participants completed the 14-day diary; 50% were women and median age was 54 years (IQR = 43–66). Average daily pain intensity before pain medication intake was significantly higher for patients who used opioids (5.9; 95% CI 5.7–6.2) as compared to non-opioid analgesics (4.2; 95% CI 4.0–4.5) or no pain medication (2.2; 95% CI 1.9–2.5). Controlling for pain intensity, patients using opioids were more likely to report a pain relief (OR = 1.3; 95% CI 1.1–1.8) as compared to those who used non-opioid analgesics.

Conclusion Overall, opioids appear to be effective and used as intended by the prescribing physician.

Keywords Acute pain · Pain relief · Opioids · Emergency department

Résumé

Objectifs Le traitement de la douleur aiguë après la sortie des départements d'urgence (DU) reste un défi dans le contexte de la crise des opioïdes. Notre objectif était de déterminer la proportion de patients utilisant des analgésiques opioïdes

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par rapport aux analgésiques non opioïdes après leur sortie des urgences avec une douleur aiguë, et l'association du type d'analgésique avec l'intensité moyenne de la douleur avant la prise d'analgésiques et le soulagement de la douleur rapporté.

Les méthodes Il s'agissait d'une étude de cohorte prospective de patients (DU) âgés de ≥ 18 ans souffrant de douleurs aiguës (≤ 2 semaines) et ayant reçu une ordonnance d'opioïdes à leur sortie de l'hôpital. Les patients ont rempli un journal de 14 jours évaluant le niveau d'intensité de la douleur quotidienne avant chaque prise de médicaments anti-douleur (échelle d'évaluation numérique de 0 à 10), le type d'utilisation des médicaments anti-douleur (opioïdes contre non opioïdes), et si la douleur était soulagée par les médicaments utilisés ce jour-là. Des analyses multiniveaux ont été utilisées pour comparer l'effet du type d'analgésique utilisé sur l'intensité et le soulagement de la douleur.

Résultats Au total, 381 participants ont rempli le journal de 14 jours; 50% étaient des femmes et l'âge médian était de 54 ans (EI = 43–66). L'intensité moyenne de la douleur quotidienne avant la prise d'analgésiques était significativement plus élevée chez les patients qui prenaient des opioïdes (5.9; 95% IC: 5.7–6.2) par rapport aux analgésiques non opioïdes (4.2; 95% IC: 4.0–4.5) ou à l'absence d'analgésiques (2.2; 95% IC: 1.9–2.5). En contrôlant l'intensité de la douleur, les patients utilisant des opioïdes étaient plus susceptibles de déclarer un soulagement de la douleur (OR = 1.3; 95% CI: 1.1–1.8) par rapport à ceux qui utilisaient des analgésiques non opioïdes.

Conclusion Dans l'ensemble, les opioïdes semblent être efficaces et utilisés comme prévu par le médecin prescripteur.

Clinician's capsule

What is known about the topic?

Because of the risks associated with opioid misuse, many have questioned the use of opioids for patients discharged from EDs.

What did this study ask?

When are opioids used by patients, and do they experience a difference in pain relief, as compared to non-opioid analgesics?

What did this study find?

Compared to non-opioid analgesics, opioids were consumed when pain intensity was higher and more patients reported pain relief.

Why does this study matter to clinicians?

Patients tend to follow the WHO analgesic ladder instructions (use non-opioid first) as intended by ED physicians.

non-opioid analgesics to opioids [10–14]. For example, a randomized controlled trial by Barnaby et al. [12] compared 1 g of intravenous (IV) acetaminophen with 1 mg of IV hydromorphone for the treatment of acute pain in the ED, and found that hydromorphone provided clinically and statistically better analgesia than acetaminophen 60 min after administration. In addition, two meta-analyses by Sin et al. [13, 14] found limited and flawed evidence to support the use of IV acetaminophen as an alternative to opioids for the primary management of renal colic or acute pain in the ED. Some studies did not find significant differences in pain relief between opioids and non-opioids. However, most of them were done with a short follow-up, in a secure ED setting, and for a specific acute pain problem; these studies cannot be generalized to home pain management [10, 11].

Previous studies that have evaluated the total quantity of opioids consumed during an acute pain follow-up for ED discharged patients [15], or after surgery [16] have found that the majority (68% and 58%, respectively) of the prescribed opioids were not consumed. These recent findings suggest that most of the patients suffering from acute pain are taking opioids sparingly to relieve their pain. However, no study has yet examined patients' pain intensity before they consumed an analgesic for acute pain and its association with pain relief after ED discharge.

The objective was to determine the proportion of patients using opioid vs non-opioid pain medication following discharge from the ED with acute pain, and the association of type of pain medication with average pain intensity before pain medication intake and report of pain relief. We hypothesized that pain intensity before consuming an opioid will be higher and that pain relief, after controlling for previous pain intensity, will be better than for those who consumed only non-opioids pain medications.

Introduction

The treatment of acute pain in the emergency department (ED) and after discharge remains a challenge in the opioid crisis context [1]. Because of the risks associated with opioid misuse, physicians are more cautious and try to limit the use of opioids for the treatment of acute pain in the ED [2–7]. Unlike chronic pain syndromes, where the efficacy of opioids is often questioned, opioids remain an important tool for the management of moderate to severe acute pain [8, 9], especially when other alternatives have failed to relieve patients.

To reduce the use of opioids in the context of acute pain, some studies have compared the therapeutic effect of

Methods

Study design and setting

This was a prospective cohort study on acute pain management after ED discharge from an urban, academic, tertiary care, level-1 trauma centre with an affiliated emergency medicine residency program and an annual census of approximately 65,000 ED visits (95% adults) [15]. Approval was obtained from the local institutional ethics review board.

Selection of participants

Patients aged 18 years or older treated in the ED from June 2016 to July 2017 were identified by ED physicians 24 h per day, 7 days a week. We included patients with an acute pain discharge diagnosis present for less than 2 weeks and discharged from the ED with an opioid prescription. All patients who were prescribed opioids at discharge were referred to research nurses; they then verified inclusion and exclusion criteria, explained the study, and obtained informed consent. Patients could not participate more than once. The selection of patients who received an opioid prescription was not predetermined; pain management was left to the treating physician's preference. ED physicians generally used the World Health Organisation (WHO) analgesic ladder to instruct patients how to manage their pain at home, but these instructions were not standardized. We excluded patients who did not speak French or English, were using opioid medication prior to the ED visit (preceding 2 weeks, prescribed or not), stayed in the ED for more than 48 h, or were suffering from cancer or chronic pain.

Data collection and processing

Patients' demographic information, pain intensity at triage (11-point numerical rating scale; NRS), arrival mode, triage priority, and length of ED stay were extracted from our computerized medical system. Physicians recorded on a research form, patients' final diagnosis, pain intensity at discharge (11-point NRS), and prescribed pain medications. Patients received a 14-day diary in which they recorded the quantity, time, names of all pain medications consumed daily, and the pain intensity level (11-point NRS) prior to consuming medication. Patients who did not take any pain medication during the day, were also asked to report their average daily pain level on an 11-point NRS ranging from 0 to 10, where 0 represents "no pain at all" and 10 represents "the worst imaginable pain." Pain intensity measured with NRS can be categorized as mild (0–4), moderate (5–6) and severe (7–10) [17]. Finally, all patients (using medication or not) were also asked each day: "Were

you generally relieved by the pain medication you took today?", with the option of answering "Yes", "No", "Did not take any medication". Using pre-addressed and pre-stamped envelopes, these diaries were mailed back by the patients after completion. We chose a 2-week follow-up period, because it represents a reasonable acute pain time frame definition [18] and it was also during this period that the need for pain medication was significantly resolved in a majority of patients (88%) in our pilot study [19]. Study data were entered and managed using REDCap (Research Electronic Data Capture) [20].

The average daily pain intensity prior to pain medication was calculated for each patient, after sorting by type of analgesic consumed. When patients did not consume any medication during the day, the answer to the question on average pain intensity of the day was used instead. Since pain relief was only reported once a day, it was associated to analgesics in this way: when patients consumed opioids and non-opioids during the same day, the daily pain relief was attributed to opioids. When patients consumed only non-opioids during the day, the pain relief of the day was associated with non-opioids. We choose to recode that way, since in our pilot study, almost no patients consumed only opioids during the day.

Data analysis and statistics

Baseline characteristics of patients included in the study, those who refused to participate, and those who did not return the diary are presented with descriptive statistics. We calculated differences in median and in proportion with associated 95% confidence intervals for included patients compared to the other two groups. Hodges–Lehman estimates were used to calculate 95% confidence intervals of median differences. We grouped pain conditions into four categories frequently encountered in the ED [21] and with different pain trajectories [22]; musculoskeletal, fracture, renal colic, and other pain complaints (e.g., abdominal pain, abscess, burn, tooth pain, etc.).

Differences in pain intensity between the two types of medication consumed (opioid vs non-opioid) were assessed with mixed models with two repeated factors (type of medication, and follow-up day); age and sex were also used as fixed factors and subjects as random factor. Mixed models present several advantages for repeated-measures data analysis. First, they properly account for correlation between repeated measures on the same subject and offer more flexibility in modeling time effects [23]. In addition, such models use all available data, even for patients with partial information. To evaluate the effect of type of pain medication (opioid vs non-opioid) consumed on pain relief, multilevel binary logistic regression was

used controlling for pain intensity level before pain medication intake, days of the week, age, and sex. Variance components covariance structures were used for both multilevel modelling. Alpha level was set at 0.05, and means and odds ratios (OR) were reported with their 95% confidence intervals (CI). Analyses were performed using SPSS version 25 (IBM corp.).

Results

Study cohort description

During our 1-year recruitment period, a total of 1315 patients meeting the inclusion criteria were initially contacted. Of these, almost 30% had exclusion criteria, 13% declined to participate, and 50% of those who participated returned the diary, leaving 381 participants (Fig. 1). Non-participants and included patients were similar in baseline

characteristics (Table 1). Patients lost to follow-up were significantly younger and received more NSAID prescriptions at ED discharge than included patients. Included patients' median age was 54 years, half were female, and pain intensity at triage was severe (8), decreasing to moderate (5) at ED discharge. The median number of 5 mg morphine pills equivalent prescribed at ED discharge was 30 and 95% of the patients filled their prescription. During the 14-day follow-up, 82% of the patients consumed opioids, 72% consumed acetaminophen, and 45% consumed NSAIDs.

Type of pain medication used during the 14-day follow-up after ED discharge

The proportion of opioids and non-opioids consumed during the 14-day follow-up is presented in Fig. 2 (panel A). Opioids were used by almost 70% of patients during the first 2 days and dropped to 10% at the end of the 14-day

Fig. 1 Flow chart of patients' enrollment in the study

Table 1 Baseline characteristics of patients included in the study, those who refused to participate, and those who did not return the diary (Lost to follow-up)

Baseline characteristics	Included (<i>N</i> = 381)	Refused to participate (<i>N</i> = 176)	Lost to follow-up (<i>N</i> = 380)	Difference (95% CI) included vs refused	Difference (95% CI) included vs lost
Age, median, (IQR, range), y	54 (43–66, 18–95)	53 (39–66, 18–91)	44 (35–56, 18–92)	1 (– 2 to 5)	10 (7 to 12)
Sex, %, men	50	47	56	3 (– 6 to 12)	– 6 (– 13 to 1)
ED arrival mode, %					
By self	82	76	77	6 (– 1 to 13)	5 (– 1 to 11)
By ambulance	18	24	23		
High (levels 1 or 2) triage priority, %	42	45	44	– 3 (– 12 to 6)	– 2 (– 9 to 5)
Pain intensity at triage, median, (IQR)	8 (7–9)	8 (7–10)	8 (7–10)	0 (0 to 0)	0 (0 to 0)
ED treatment section, %					
Ambulatory	66	63	63	3 (– 6 to 12)	3 (– 4 to 10)
On stretcher	34	37	37		
Type of pain conditions, %					
Musculoskeletal	45	41	42	4 (– 5 to 13)	3 (– 4 to 10)
Fracture	19	23	18	– 4 (– 11 to 2)	1 (– 5 to 7)
Renal colic	17	19	17	– 2 (– 9 to 5)	0 (– 5 to 5)
Other	20	17	23	3 (– 4 to 10)	– 3 (– 9 to 3)
Acetaminophen [†] prescriptions at ED discharge, %	72	69	72	3 (– 5 to 11)	0 (– 6 to 6)
NSAID prescriptions at ED discharge, %	41	43	53	– 2 (– 11 to 7)	– 12 (– 19 to – 5)
Opioid [‡] prescription types at ED discharge, %					
Morphine	43	42	44	1 (– 8 to 10)	– 1 (– 6 to 6)
Oxycodone	41	36	40	5 (– 4 to 14)	1 (– 6 to 8)
Hydromorphone	18	22	15	– 4 (– 11 to 3)	3 (– 2 to 8)
No. of morphine 5 mg equivalent pills prescribed, median, (IQR)	30 (20–45)	30 (20–45)	30 (20–48)	0 (– 1 to 3)	0 (– 1 to 2)
ED stay duration, median, (IQR), h	5 (4–8)	6 (4–8)	5 (4–8)	– 1 (– 1 to 0)	0 (– 1 to 0)
Pain intensity at ED discharge, median, (IQR)	5 (2–7)	5 (2–7)	5 (2–7)	0 (0 to 1)	0 (0 to 0)

IQR interquartile range, NSAID nonsteroidal anti-inflammatory drug

[†]Acetaminophen was always prescribed or verbally suggested separately from opioids (no combinations)

[‡]Hydrocodone is not used for pain management in Canada

follow-up. Conversely, 10% of patients did not use any medication to relieve their pain on the first day after ED discharge; at day 14, almost 70% were not using pain medications. The percentage of patients taking NSAIDs and/or acetaminophen decreased throughout the 14 days but remained higher than for those using opioids.

Pain intensity before pain medication consumption

Patient's average pain intensity over time, prior to pain medication use, is shown in Fig. 2 (panel B). Mixed model

analysis revealed that pain intensity prior to pain medication use was significantly higher for opioids users (5.9; 95% CI 5.7–6.2) as compared to patients who used non-opioids (4.2; 95% CI 4.0–4.5) or no pain medication (2.2; 95% CI 1.9–2.5) ($p < 0.001$) (Fig. 3). It also showed a decrease in pain intensity throughout the 14 days of follow-up for all types of pain medication ($p < 0.001$) and that women reported significantly higher pain intensity (mean difference: 0.5; 95% CI 0.2–0.8) than men before pain medication intake ($p < 0.001$). No age or interaction effects were significant.

Fig. 2 The 14-day diary evolution of the percentage of patients using each type of pain medication (a), of mean pain intensity ($\pm$ SEM) before each type of pain medication consumption (b), and of the percentage of patients reporting pain relief for opioids and for NSAIDs-Acet only (not adjusted for pain intensity, age and sex) (c); NSAIDs-Acet: Nonsteroidal anti-inflammatory drugs and/or acetaminophen

Pain relief from pain medication consumption

Unadjusted patients' pain relief for the two types of pain medications during the 14 days are shown in Fig. 2 (panel

Fig. 3 Association between the type of pain medication and reported pain intensity (mean $\pm$ SEM) just before the medication intake; NSAIDs-Acet: Nonsteroidal anti-inflammatory drugs and/or acetaminophen; No Med.: No pain medication consumption

C). Pain relief for opioid and non-opioid analgesics users was good and relatively stable throughout the 14-day follow-up period, with 75–95% of the patients reporting relief. Using multilevel binary logistic regression, controlling for previous pain intensity, age, sex, and follow-up day, patients using opioids were overall more likely to be relieved (OR = 1.3; 95% CI 1.1–1.8) compared to those who used NSAIDs and/or acetaminophen. Women were more likely to report relief compared to men (OR = 1.4; 95% CI 1.1–1.8) and older patients were also more likely to report relief from pain medication compared to younger patients (OR = 1.5; 95% CI 1.2–2.0). No significant effect of the follow-up day, or interaction between day and type of medication on pain relief were observed during the 14-day follow-up ($p > 0.30$).

Discussion

Interpretation

This prospective, cohort study showed that the proportion of patients using pain medication demonstrated a linear decrease across the 14-day follow-up, with faster decrease for opioid users as compared to non-opioid users. Patients who consumed opioids reported higher average pain intensity scores as compared to those who used non-opioid analgesics or no pain medication. Furthermore, patients who used opioids were more likely to report relief of pain after controlling for pain intensity prior to pain medication intake.

A large proportion of patients filled their prescription and used opioids in the first 2 days following ED discharge when the pain was rated at its worst. This proportion of opioid

use decreased linearly until the end of the follow-up period and is related to the decrease in pain intensity. Additionally, the proportion of patients using non-opioids pain medication remained higher compared to those using opioids during the entire follow-up and patients tend to consume only non-opioids pain medication when pain intensity decreases; this suggests that patients tend to follow the WHO ladder instructions given by the ED physicians.

Previous studies

Patients who used opioids reported significantly higher pain intensity before medication intake compared to those who used non-opioid analgesics or those who did not take any pain medication. That difference was statistically and clinically significant as it exceeded the 1.3 difference established in the NRS validated definition [24, 25]. It is also important to note that this difference in pain intensity persisted through the 14-day follow-up period. This suggests that patients who still used opioids at the end of the follow-up were in moderate or severe pain. Still, the average initial pain after ED discharge of patients who took non-opioid analgesics was of moderate intensity. Thus, patients try to manage moderate pain intensity without opioids. They also seem to stop taking opioids when their pain intensity is lower, and has shown in other studies possibly also because of fear of addiction or side effects [26]. A previous study showed that side effects are indeed prevalent during short-term opioid treatment for acute pain [27].

Pain relief for opioid and non-opioid analgesics users was good and relatively stable throughout the 14-day follow-up period. Though, during the first 4 days of follow-up, the percentage of pain relief seems to be higher with NSAIDs and/or acetaminophen. However, when adjusting for the level of pain before medication ingestion, which was higher for opioid users, pain relief was 34% more likely with opioids than with non-opioid analgesics. This result is similar to other studies showing the advantage of using opioids to relieve moderate to severe acute pain [12–14].

As previously shown, women in our study reported statistically significant higher pain intensity before medication ingestion than men [28–32]. However, that difference was low (0.5) and was not clinically significant based on the standard of a NRS 1.3 difference [24, 25]. A higher proportion of women also reported pain relief as compared to men; this finding was previously described in a study of older women [33]. Patients aged 65 years and over reported similar pain intensity as younger patients before consuming medication, which is consistent with older patients reporting comparable pain intensity for similar painful conditions [34]. However, they reported higher levels of pain relief compared to younger patients, something that has also been previously reported [35].

Limitations

This study has limitations: it was done at a single site, an urban, academic, tertiary care hospital, and thus its findings may not generalize to other healthcare settings. The low diary return rate obtained in the present study (50%) could also bias our sample representativeness. However, we did not find significant differences in baseline characteristics (Table 1) between patients who completed the study and those who did not. In addition, since patients were only asked about their pain relief once a day, it is possible that pain relief was due to the co-analgesic effect when patients consumed opioids and acetaminophen and/or NSAIDs during the same day. Asking patients to average their daily pain intensity when no pain medication was consumed could also introduce measurement bias, since their pain probably fluctuated during the day depending on activity and other variables. Furthermore, self-reported opioid use and reported pain intensity could be biased by social desirability issues. Nonetheless, studies have shown the validity of self-reporting illicit substance usage with urine drug screen confirmation [36–38].

Clinical and research implications

In the opioid crisis context, physicians are more cautious and try to limit the use of opioids [2–7]. However, our data supports the use of opioids for acute pain; on their own, patients use them for more severe pain, for which they provided better relief than non-opioid analgesics alone, and generally their intake was gradually stopped during the 14-day follow-up. Furthermore, patients usually consumed opioids sparingly during the acute pain period after an ED visit [15]. However, there are known limitations and risks with the use of opioids for acute pain. They are commonly associated with side effects [27] and, in a small proportion of patients, misuse following an ED visit [39]. Opioids should continue to be considered for use in acutely painful conditions, particularly for patients with moderate to severe pain, as they appear to be more effective than non-opioid pain medication. But physicians should be aware that withdrawal symptoms have been demonstrated in humans and animals after a single opioid dose [40], this could lead to substance use disorder [41, 42]. Moreover, leftover opioids are the main supply of prescription pills for misuse; therefore, physicians should prescribe the appropriate quantity of opioids to relieve pain while limiting unused pills [15] and avoid them if patients have risk factors for substance use disorders [43]. Future prospective multi-center studies measuring pain intensity before and after each pain medication consumption, evaluating patients' satisfaction and beliefs about taking opioids or pain relief, identifying risk factors for substance use disorders, and examining nonpharmacological modalities to treat

pain should increase our understanding of acute home pain management.

Conclusion

Following ED discharge for an acutely painful diagnosis, patients generally used opioids when the pain was reported as more severe and were more likely to report pain relief than non-opioid pain medications. The vast majority of patients stop taking opioids at the end of a 2-week follow-up period. Overall, opioids appear to be effective and used as intended by the prescribing physician. However, this does not exclude the possibility of developing a substance use disorder.

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Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to declare.

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