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SUBCUTANEOUS FENTANYL ADMINISTRATION: A NOVEL APPROACH FOR PAIN MANAGEMENT IN A RURAL AND SUBURBAN PREHOSPITAL SETTING

Johann Lebon, PhD, Francis Fournier, MD, François Bégin, MD, FRCPC, Denise Hebert, BcSc-Inf, Richard Fleet, PhD, MD, CCMF, Guillaume Foldes-Busque, PsyD, PhD, Alain Tanguay, MSc, MD

ABSTRACT

Objective: To determine the feasibility, safety, and effectiveness of the subcutaneous route of fentanyl administration by Basic Life Support–Emergency Medical Technicians (BLS-EMT) in a rural and suburban region, with the support of an online pain management medical control center. Methods: Retrospective study of patients who received subcutaneous fentanyl and were transported by BLS-EMT to the emergency department (ED) of an academic hospital between July 1, 2013 and January 1, 2014, inclusively. Fentanyl orders were obtained from emergency physicians via an online medical control (OLMC) center. Effectiveness was defined by changes in pain scores 15 minutes, 30 minutes, and 45+ minutes after initial fentanyl administration. Safety was evaluated by measuring vital signs, Ramsay sedation scores, and adverse events subsequent to fentanyl administration. Feasibility was defined as successful fentanyl administration by BLS-EMT. SPSS-20 was used for descriptive statistics, and independent t-tests and Mann-Whitney U tests were used to determine inter- and intra-group differences based on transport time. Results: Two hundred and eighty-eight patients (288; 14 to 93 years old) with pain scores ≥7 were eligible for the study. Of the 284 (98.6%) who successfully received subcutaneous fentanyl, 35 had missing records or data, and 249 (86.5%) were included in analyses. Average pain score pre-fentanyl was 8.9 ± 1.1. Patients <70 years old received a higher dose of fentanyl than those ≥70 years old (1.4 ± 0.3 vs. 0.8 ± 0.2 mcg/kg, p < 0.05). Pain scores decreased significantly post-fentanyl administration and the proportion of patients achieving pain relief increased significantly (p < 0.05) over the course of transport to ED (15 minutes, 30 minutes, 45+ minutes). Only 1.6% of patients experienced adverse events, including hypotension (n = 2; 0.8%), nausea (n = 1; 0.4%), and Ramsay level >3 (n = 1; 0.4%). Conclusion: Prehospital subcutaneous fentanyl administration by BLS-EMT with the support of an OLMC center is a safe and feasible approach to pain relief in prehospital settings, and is not associated with major adverse events. Effectiveness, subsequent to subcutaneous fentanyl administration is characterized by a decrease in pain over the course of transport to ED. Further studies are needed to compare the effectiveness of SC administration by EMS with other routes of administration and other analgesics. Key words: Basic Life Support; fentanyl; pain management; prehospital; subcutaneous administration

INTRODUCTION

Major North-American prehospital and emergency medicine organizations including the National Association of Emergency Medical Services Physicians (NAEMSP), American College of Emergency Physicians (ACEP), and Canadian Association of Emergency Physicians (CAEP) acknowledge that formal pain assessment and timely analgesic administration are essential for optimal pain management. Among diverse analgesics (e.g., morphine, fentanyl, methoxyflurane, ketamine, and acetaminophen) and methods of analgesic administration described in the literature,
intravenous (IV),6,8,12 and intranasal (IN)11,13—15 fentanyl administration have been established as the most common methods for pain management in prehospital settings worldwide.

The literature also indicates that the IV and IN routes for opioid administration are not always feasible or effective for pain management in prehospital settings.13,16—18 Studies have revealed that only 1.8 to 18.9% of patients eligible for pain relief receive some form of prehospital analgesia.8,12,19,20 In addition, cannulation (IV) may be associated with technical problems that can prevent successful opioid administration,16,17 as cannulation only occurs in up to 22% of patients transported by ambulance.17,21 The latter can create significant delays in analgesic administration during ambulance transport,16,17 thereby preventing patients from receiving adequate pain relief prior to ED arrival.16,17,22 Regarding IN administration, a recent review concluded that there exists only limited quality evidence to support its use in ED (8 studies) and prehospital (4 studies) settings due to low scientific quality of studies performed in these settings and thus, further controlled and randomized trials are required to validate its use.18 Consequently, IN opioid administration is thus not necessarily optimal nor should be recommended as routine care for pain management so far.

Since each emergency medical services (EMS) system is unique, many jurisdictions do not authorize Basic or Advanced Life Support-Emergency Medical Technicians (BLS-EMT or ALS-EMT) to administer IV or IN analgesics as routine practice. Even authorized BLS and ALS may be limited by insufficient training, and may lack the experience required to successfully recognize, treat, and control pain with intravenous or naso5,16,19,23,24 administration of analgesia. Disparities in BLS or ALS experience, skill, and knowledge may also be attributable to practice setting (i.e., rural vs. urban).16,23,24

Given that a significant proportion of patients in worldwide EMS systems are transported from the field to ED by BLS-EMT and given the aforementioned points, alternatives to IV or IN opioid for analgesic administration and pain management by BLS-EMT in prehospital settings could significantly improve pain relief practice. Subcutaneous (SC) analgesic administration is a proposed option that has been established as an effective and safe alternative to IV and IN administration in hospital settings. Although the SC route results in a relatively delayed analgesic onset and requires the use of a needle, the advantages of SC administration in prehospital settings includes avoiding venous access, as well as problems associated with intranasal administration.18,25 Additionally, subcutaneous administration has been demonstrated to be more convenient, and associated with greater patient satisfaction25,26 than is IV administration. Given these findings, it is surprising that SC administration has not yet been formally studied in prehospital setting.

The objective of the present study was to evaluate the feasibility, safety, and effectiveness of subcutaneous fentanyl administration by BLS-EMT in a rural and suburban prehospital setting with the support of an online medical control center.

**METHODS**

**Study Design**

This study constitutes a retrospective analysis of a clinical innovation in pain management established in a rural and suburban prehospital setting in Levis, Quebec, Canada that involved BLS-EMT supported by a regional online medical control (OLMC) center called the Unité de Coordination Clinique des Services Préhospitaliers d’Urgence (UCCSPU) [Prehospital Care Clinical Coordination Unit]. The UCCSPU is located in the ED of the Hôtel-Dieu de Lévis academic hospital (HDL).27 The project was approved by the research ethics committee of the Centre de Recherche de l'Hôtel-Dieu de Lévis [Hôtel-Dieu de Lévis Research Center].

The objective of the UCCSPU is to provide online medical support and assistance to BLS-EMT in the Chaudière-Appalaches region (4,764 km²), home to approximately 400,000 residents. Details concerning the role of the UCCSPU in pain management have been published elsewhere.27 In brief, patients in this area who requested EMS were evaluated in the field by BLS-EMT using specific protocols based on presenting complaint and condition. After evaluation, patients reporting pain were asked to rate their pain on a verbal numeric rating scale (VNRS, 0-10 pain score). If they reported a pain score equal to or greater than 7 on the VNRS and requested pain relief, BLS-EMT contacted the OMLC physicians to request a fentanyl order via a direct telephone line. OLMC physicians evaluated patients’ clinical information as per the established analgesia protocol, to confirm patients’ eligibility for fentanyl administration, and then to order a fentanyl dose for subcutaneous administration by BLS-EMT. The latter administered the appropriate dose of fentanyl into the patient’s upper limb using a 23-gauge needle. Finally, a post-medication monitoring protocol was implemented until the ambulance arrived at the ED.

As previously described,24 the majority of BLS-EMT in the Chaudière-Appalaches region have been administering subcutaneous fentanyl since July 2010, in the context of a pilot project. The project involved a detailed analgesic protocol for legal administration of subcutaneous fentanyl for pain management in patients with a variety of presenting conditions transported by ambulance in the rural and suburban region.
of Levis, Quebec. The project was supervised by the UCCSPU. The Collège des Médecins du Québec [Quebec College of Physicians] approved subcutaneous administration as the route and fentanyl as the analgesic of choice for this pilot project.24 Fentanyl was chosen for its advantageous pharmacokinetic and pharmacodynamic properties, including: 1) a relatively rapid rate of absorption; 2) a 15-minute median action time (range 10–30 minutes); and 3) a short half-life.28–30 BLS-EMTs completed an intensive 4-hour training that allowed them to implement the pain management protocol and to manage controlled substances. The UCCSPU provided support and assistance to ensure compliance to the protocol.

Study Population and Setting

This study analyzed data from the first six months of full implementation of the clinical pain management protocol (July 1, 2013 to January 1, 2014, inclusively). Eligible cases were selected from ambulance and UCCSPU patient care records from the period outlined above.

Inclusion criteria were patients: 1) being transported by ambulance from the scene of the incident to HDL; 2) pain level of 7 or greater on the VNRS31; and 3) analgesic requested by both patients and BLS-EMT. Exclusion criteria were patients: 1) under 14 years of age32; 2) categorized as P or U on the AVPU consciousness scale (i.e., Alert, responsive to Painful stimulation, or Unresponsive) by BLS-EMT33; 3) known allergy to fentanyl; 4) systolic blood pressure (SBP) under 100 mmHg; 5) respiratory rate (RR) under 12 breaths/min; and 6) headache as chief complaint. Being on regular medication and having taken medication (e.g., acetaminophens, anti-inflammatories, etc.) prior to calling EMS were not criteria for exclusion.

Study Protocol

The analgesia protocol authorized BLS-EMT to administer subcutaneous fentanyl during ambulance transport, upon decision of fentanyl orders with the UCCSPU emergency physician’s approval. The protocol involved a maximum first dose of 1.5 microgram/kg of body weight (mcg/kg) for patients between 14 and 70 years old. Patients in this age range could receive additional doses every 30 minutes as needed, if all inclusion and exclusion criteria were met. Most ambulances took under 60 minutes to arrive at ED, so patients received a maximum of two doses during ambulance transport. For patients 70 years or older (≥70), the initial and maximum dose was 50 mcg, as established by the Collège des Médecins du Québec.24 Patients were subject to serial clinical monitoring post-fentanyl dose, to identify vital sign abnormalities or adverse events.

Measurement

Data from EMS and UCCSPU records were used to determine the feasibility, safety, and effectiveness of subcutaneous fentanyl administration by BLS-EMT. More specifically, feasibility was measured by the rate of successful fentanyl administration (proportion of patients that received analgesic) by BLS-EMT and by data concerning problems encountered during the process.

Analgesic effectiveness was characterized by decrease in pain score on the 0-10 VNRS pain scale31 at 15 minutes, 30 minutes, and 45+ minutes after fentanyl administration. Analgesic effectiveness was also defined by the clinically significant pain relief (CSPR) score that is determined as a minimum post-treatment reduction of 1.5 (some effect) or 3 (effective) points on the VNRS by reviewing analgesic records. CSPR scores are commonly used in pain studies and are considered to be appropriate indicators of analgesia effectiveness.34–37 We used two effectiveness indicators in order to separate patients into three categories based on changes between initial and final pain intensity36: 1) patients with no improvement and categorized as “ineffective” with a reduction smaller than 1.5 points on the VNRS (VNRS < 1.5); 2) patients with a minimal improvement and categorized as having “some effect,” with a reduction between 1.5 and 3 points on the VNRS (1.5 ≤ VNRS < 3); and finally, 3) patients with significant improvement and categorized as “effective,” with a reduction on the VNRS equal to or greater than three points (VNRS ≥ 3).

Fentanyl safety was defined by an absence of adverse events or abnormal vital signs noted by BLS-EMT or complaints reported by patients. Adverse events were considered major if they required BLS-EMT intervention such as intubation, respiratory assistance, or naloxone administration, and were considered minor if clinical intervention was not necessary (e.g., nausea, symptomatic hypotension, or vomiting). Vital signs, including systolic blood pressure (SBP, mmHg), respiratory rate (RR, breath/min), pulse (min), and level of consciousness (AVPU scale)35 were measured before (pre) and every 15 minutes after (post) subcutaneous fentanyl administration until ED arrival. Oxygen saturation (SpO2, %) was measured after fentanyl administration. Abnormal signs included SBP under 100 mmHg, RR under 12 breaths/min, SpO2 below 92%, pulse under 50/min, and rating of P or U on the AVPU scale. Level and effectiveness of sedation were measured every 15 minutes after fentanyl administration using the 6-level Ramsay scale, which describes six possible states of consciousness subsequent to drugs administration. The levels are based on ability to respond to auditory or tactile stimuli.38,39
Finally, elapsed time between subcutaneous fentanyl administration and ED arrival was calculated using BLS-EMT prehospital charts and records. This variable was used to compare the safety and effectiveness of subcutaneous fentanyl administration at the different measurement points.

**Statistical Analyses**

Results are presented as means ± standard deviations (tables) or error bar +/- 2 S.D (figures). Parametric analyses were performed on all normally distributed variables of interest; nonparametric analyses were performed for ordinal and nonnormally distributed variables. Independent t-tests were used for descriptive statistics for each variable for each age group. We also used independent t-tests to explore differences between the two age groups (< 70 or ≥ 70 years old), given that they received different doses of fentanyl. The Mann-Whitney U test was used to explore between-group differences on ordinal variables. Difference in pain score between pre- and post-fentanyl administration and between post-administration time points (15 minutes, 30 minutes, and 45+ minutes post-administration) were calculated using nonparametric tests (Two related samples test). The P values < 0.05 were considered statistically significant. All analyses were performed using SPSS 20.0 (Chicago, IL, USA).

**RESULTS**

Of the 6422 patients transported by ambulance during the study period, 288 (4.5%) fulfilled the requisite criteria for BLS-EMT to request pain relief, and 284 patients (284/288; 98.6%) received subcutaneous fentanyl. However, data from 35 of the 284 patients were excluded due to: 1) missing prehospital records (n = 3) or 2) missing post-administration pain score (n = 32). In the end, data from 249 (87.7%; 121 men and 128 women) patients between 14 and 93 years of age (mean ± S.D = 55.8 ± 20.8 years old) were included in the analyses (Figure 1).

Participants’ baseline characteristics are presented in Table 1. Significant differences (p < 0.05) between age groups (< 70 years old vs. ≥ 70 years) were observed for gender and weight. Mean pain score prior to fentanyl administration (i.e., at baseline) for the two groups was 8.9 ± 1.1; no significant difference between age groups was observed (p > 0.05; 8.9 ± 0.8 vs. 8.9 ± 1.1). Patients < 70 years old received a higher dose of fentanyl (1.4 ± 0.3 mcg/kg) than did those aged ≥ 70 years old (0.8 ± 0.2 mcg/kg), as per the fentanyl administration protocol.

Table 2 lists patients’ presenting pain conditions. The majority of patients receiving fentanyl for pain relief reported trauma (38.6%), abdominal pain (28.1%), and back or neck pain (19.3%). There was no difference in presenting condition between the two age groups. The respective proportions reporting trauma, abdominal pain, and back or neck pain were 41.1%, 29.1%, and 18.3% for patients < 70 years old, and 32.4%, 25.7% and 21.6% for patients ≥ 70 years old (Table 2).

Of the 249 patients included in this study, 15 (6%) received an additional dose of fentanyl (Figure 1), but no major adverse events were reported (Table 3). Where safety was concerned after fentanyl administration, only four patients reported minor events: two patients (≥70 years), had a SBP < 100 mmHg (90 and 99 mmHg); one patient (<70 years) had a Ramsay level > 3 (Ramsay = 4); and one patient (≥70 years) reported

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**Figure 1.** Flow chart of the patients retrieved, excluded and included in the study.
TABLE 1. Baseline characteristics of subjects

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Below 70 years old</th>
<th>70 years old &amp; over</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean</td>
<td>Mean</td>
</tr>
<tr>
<td>Age (years)</td>
<td>249</td>
<td>55.8 ± 20.8</td>
<td>74 79.8 ± 6.6*</td>
</tr>
<tr>
<td>Sex (male; %)</td>
<td>249</td>
<td>121; 48.6</td>
<td>25; 33.8*</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>248</td>
<td>74.5 ± 17.7</td>
<td>73 67.9 ± 14.8*</td>
</tr>
<tr>
<td>Mean Pain Score Pre-</td>
<td>249</td>
<td>8.9 ± 1.1</td>
<td>74 8.9 ± 1.1</td>
</tr>
<tr>
<td>Fentanyl administered</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total dose of fentanyl</td>
<td>249</td>
<td>1.2 ± 0.4</td>
<td>72 0.8 ± 0.2*</td>
</tr>
</tbody>
</table>

*p < 0.05: significant difference between <70 years old and equal or over 70 years old.

**Table 2. Patients’ conditions leading to analgesic**

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Below 70 years old</th>
<th>70 years old &amp; over</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Trauma</td>
<td>96 (38.6)</td>
<td>72 (41.1)</td>
<td>24 (32.4)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>70 (28.1)</td>
<td>51 (29.1)</td>
<td>19 (25.7)</td>
</tr>
<tr>
<td>Heart related pain</td>
<td>4 (1.6)</td>
<td>3 (1.7)</td>
<td>1 (1.4)</td>
</tr>
<tr>
<td>Other chest pain</td>
<td>4 (1.6)</td>
<td>3 (1.7)</td>
<td>1 (1.4)</td>
</tr>
<tr>
<td>Back and neck pain</td>
<td>48 (19.3)</td>
<td>32 (18.3)</td>
<td>16 (21.6)</td>
</tr>
<tr>
<td>Others Pain</td>
<td>27 (10.8)</td>
<td>14 (8.0)</td>
<td>13 (17.6)</td>
</tr>
</tbody>
</table>

Back and neck pain: lumbar, dorsal and cervical pain; other pain: general, legs, fingers pain; non-heart pain: chest pain not associated to heart.

**Table 3. Effect expected and obtained after fentanyl administration and subcutaneous injection**

<table>
<thead>
<tr>
<th>Expected adverse events</th>
<th>Total</th>
<th>&lt;70 years old</th>
<th>≥ 70 years old</th>
<th>Obtained adverse events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subcutaneous Injection</td>
<td></td>
<td></td>
<td></td>
<td>Unsuccessful injection</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>No of problems associated to injection</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fentanyl Administration</td>
<td></td>
<td></td>
<td></td>
<td>Systolic Blood Pressure (SBP) &lt;100 mmHg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Respiratory rate &lt;12 breath/min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SpO2 &lt;90%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pulse &lt;50/min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Being “P” or “U” on AVPU scale</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ramsey level &gt; 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Allergic reaction to fentanyl</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Nausea</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Vomiting</td>
</tr>
</tbody>
</table>

<70: under 70; ≥70: equal and over 70; n: number of person; (4): data in brackets are the value of each adverse event.

**Table 3.** Effect expected and obtained after fentanyl administration and subcutaneous injection

CSPR < 3), the proportion of patients who reported relief increased only slightly from 15 minutes (19.3%; 48/249) to 30 minutes (20.0%; 26/130) post-fentanyl administration. It must be mentioned that 51% of patients experienced no significant pain relief (CSPR < 1.5) at 15 minutes post-fentanyl administration but that

**Figure 2.** Pain score before (pre) and after (post) administration of fentanyl. *p < 0.05: significant different between Pre-Fentanyl and, 15, 30, and +45 Post-Fentanyl administration, respectively (Paired t-Test); Error bar = +/− 2 SD; (*): dark full line, minimal pain score for fentanyl administration; 45+min = times that includes all measures taken at and after 45 minutes.
Intravenous (IV) analgesic administration is widely used in prehospital settings and has been demonstrated to have several advantages; our data suggest that the subcutaneous route may constitute a valid alternative to IV administration. In particular, subcutaneous administration circumvents problems obtaining IV access during ambulance transport. Problems with IV access are common and can prevent patients from receiving appropriate pain relief regardless of EMT level of experience or region of service. Indeed, in the present study, 99.3% (286/288) of patients who were eligible for pain relief successfully received subcutaneous analgesia without any problems. In contrast, the literature demonstrates that, for IV administration, only 22% of eligible patients successfully received analgesia. Together, these findings confirm that, in comparison with IV administration, the SC route is a convenient and safe alternative approach to pain relief in prehospital settings in jurisdictions where BLS-EMT are not authorized to perform IV cannulation.

This approach can be easily and properly performed by BLS-EMT transporting patients with diverse conditions from the field to the ED in a rural and suburban region. Indeed, our results confirmed that BLS-EMT: 1) are able to identify patients with significant pain and establish degree of pain using the pain scale; 2) can properly implement the pain management protocol; 3) have the requisite skills to administer fentanyl dose as prescribed by OLMC physicians (statement supported by the finding that 99.3% of patients in this study received subcutaneous fentanyl without any technical problems) (Figure 1); and 4) are able to appropriately monitor patients post-fentanyl administration and to follow the relevant laws for opioid use (management, use, and waste). For the present study, a four-hour training program was used and was sufficient for BLS-EMT in prehospital pain management.

Where for intranasal (IN) administration, it has been widely studied and has been proposed as a valuable, effective, and noninvasive alternative to IV administration in prehospital settings. IN has also been demonstrated to deliver adequate pain relief relative to time of onset. Thus, it may not be clear why we would propose SC as a novel means for improving pain management in this setting. The literature in this area has revealed some limitations associated with the IN route, including the unknown proportion of the dose absorbed by the nasal mucosa, the optimal dosage or number of intranasal administrations needed to obtain the appropriate concentration, mucosal irritation, possible atomizer malfunction, and even the elevated cost of the atomizer. Furthermore, given the fact that further studies are needed to validate the use of IN, the subcutaneous route seems

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**TABLE 4. Clinically significant pain relief according to time of reevaluation post-fentanyl administration**

<table>
<thead>
<tr>
<th>Clinically significant pain relief</th>
<th>Time post-fentanyl</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>15 minutes (n = 249)</td>
<td>30 minutes (n = 130)</td>
</tr>
<tr>
<td>Ineffective (n; %)</td>
<td>127 (51)</td>
<td>53 (40.8)</td>
</tr>
<tr>
<td>Some effect (n; %)</td>
<td>48 (19.3)</td>
<td>26 (20)</td>
</tr>
<tr>
<td>Effective (n; %)</td>
<td>74 (29.7)</td>
<td>51 (39.2)</td>
</tr>
</tbody>
</table>

Ineffective = CSPR < 1.5 points; Some effect = 1.5 points ≤ CSPR < 3 points; Effective = CSPR ≥ 3 points.

this proportion of patients decreased as travel time increased (Table 4).

**DISCUSSION**

The objective of the present study was to explore a novel alternative approach for pain management through fentanyl administration in a prehospital setting. We sought to establish the feasibility, effectiveness, and safety of subcutaneous fentanyl administration by BLS-EMT with the support of an online medical control (OLMC) center.

To our knowledge, the present findings are the first to demonstrate that the subcutaneous route is: 1) a feasible technique for administering medication to patients with various presenting conditions, with few reported problems; 2) an approach that can be successfully implemented during ambulance transport by BLS-EMT in a rural and suburban region, with the support of an OLMC; 3) an effective and novel alternative for achieving significant pain reduction; and 4) a safe means of administering analgesic with a very low rate of adverse effects. The results suggest that subcutaneous administration could constitute a valuable novel and alternative method to intravenous and/or intranasal administration for BLS-EMT in rural and suburban prehospital settings to provide pain management with the support of an OLMC center.

The feasibility of subcutaneous opioids administration in the hospital setting has already been established by several studies; in contrast, literature on subcutaneous administration in the prehospital setting is almost nonexistent. However, at least four studies of diverse analgesics (e.g., fentanyl, morphine, or tramadol) and diverse populations (cancer, critically ill, etc.), have yielded results that demonstrate the feasibility and safety of the SC route for pain management. Subcutaneous administration has also been demonstrated to be a safe and a suitable method of pain management for various clinical conditions (childbirth, stoke, etc.) and may constitute a novel approach for improving pain management in remote and rural settings.
to be a valid alternative method for fentanyl administration, in spite of delayed analgesic onset and the necessity of needle use (as in IV). Our data demonstrate that, regardless of EMT level of skill and experience, the four hours constitutes a sufficient training for EMTs in a rural and suburban prehospital setting to learn to successfully execute the pain management protocol.

To our knowledge, we are the first group to investigate the safety and effectiveness of the subcutaneous route for analgesia administration in a prehospital setting. Indeed, concerning fentanyl in prehospital settings, our results confirmed established findings: we found that fentanyl decreases pain without causing significant adverse events that could affect patients' condition upon ED arrival.1,5,28,30,58–60 This conclusion was supported by the following findings: 1) patients' level of consciousness was “A” or “V” on the AVPU consciousness scale upon arrival at the ED admissions center; and 2) no medical supports (e.g., intubation, respiratory support, or naloxone administration) were required during ambulance transport or upon ED admission, as all minor adverse events resolved spontaneously. It has to be mentioned that our results using fentanyl doses of 1.5 mcg/kg were consistent with the results of studies that used lower (1 mcg/kg)28 or higher (1–2 mcg/kg)3 doses (results not shown).

Our results also demonstrated that the proportion of patients that achieved clinically significant pain relief (i.e., significant and effective clinical improvement in pain level) is correlated with time elapsed between fentanyl administration and ED arrival. Degree of pain relief was not related to patients' initial presenting condition. Indeed, independently of presenting condition during ambulance transport (e.g., trauma, abdominal, or back and neck pain), the proportion of patients who reported clinically significant pain relief (characterized as “effective”) increased from 15 minutes post-fentanyl administration to 45+ minutes post-fentanyl administration (trauma = 34.4% to 41.2%; abdominal = 24.3% to 33.3%; back and neck pain = 33.3% to 57.1%). As per prior research, the elevated proportion (51%) of patients who did not achieve clinical improvement (CSPR <1.5) 15 minutes post-administration may be attributable to the onset of action of fentanyl, which studies estimate at 10 to 30 minutes with a median of 15 minutes. Thus, the effect may not have been initiated by 15 minutes in all patients.28–30 This may explain the difference in proportion of patients for whom analgesia was characterized as “ineffective,” “some effect,” and “effective” after 15 minutes, 30 minutes, and 45+ minutes. This result may also suggest that a stronger fentanyl dose would increase the proportion of patients reporting significant pain relief. But, such an increase could conceivably be accompanied by an increase in adverse events, and thus more prospective and comparative studies are needed to investigate this concern. Regarding the technique’s safety, it is supported by our finding that only 1.6% of all subjects experienced minor adverse events (one nausea, four increased Ramsay level, and two slight SBP decreases), none of which required reversal narcotic or recovery interventions, and all of which fully resolved before arrival at the ED. Thus, our results confirm the safety and effectiveness of the use of subcutaneous fentanyl for pain management in a prehospital setting. This easy and feasible approach can be rapidly implemented by BLS-EMT supported by an OLMC center.

Despite our positive results, some limitations related to the study design and objectives must be mentioned. First, the observational nature of the study did not allow us to address potential mechanisms or to discuss the pharmacokinetics of the subcutaneous route for fentanyl administration for pain management. Second, the absence of a control group did not permit comparisons between groups. Further investigations, including randomized controlled trials, are therefore needed in order to confirm our results and to validate the use of the subcutaneous route as an alternative to the intranasal route, a non-invasive option with an established shorter time of onset. Third, our sample size was small in comparison to other pain management studies, limiting statistical power. Fourth, the retrospective design may have resulted in BLS-EMT under-reporting adverse events that arose during ambulance transport or during the first hour post-ED admission. Fifth, final numeric pain scores were missing for 12.3% of participants (35/284 patients; Figure 1). This rate of missing data is nonetheless lower than that reported in other prehospital pain management studies and is primarily attributable to early ED arrival, that is, arrival before the first monitored pain score and before sedation (6.4%). Finally, given the elevated proportion of patients that reported no clinically significant pain relief (independent of presenting condition), it is possible that the fentanyl dose used in this study may not be suitable for the subcutaneous route.

Despite limitations in the study design and objectives, several strengths must be mentioned. First, ours is the first study to evaluate administration of analgesia via the subcutaneous route by BLS-EMT in a prehospital setting, with the support of an OLMC center. Subcutaneous administration seems to be both simple and feasible: 99.3% (286/288) of patient requests for pain relief were accepted and 98.6% (284/288) successfully received subcutaneous fentanyl. In contrast, in studies of IV fentanyl administration, only 22% of patients successfully have a cannulation and therefore analgesia. Finally, our study expands upon previous pain research in prehospital settings by exploring the capacity of paramedics with BLS training to implement a new protocol in a rural and suburban region.

From a clinical standpoint, subcutaneous fentanyl administration in prehospital settings can be considered to be a new, simple, convenient, and safe method
of pain management by EMS, and a viable alternative to intravenous or intranasal administration. Early analgesic intervention may increase patient comfort during ambulance transport and increase the likelihood of patient cooperation and responsiveness upon ED arrival.

CONCLUSION

The subcutaneous route for fentanyl administration is a feasible and simple alternative pain management practice applicable in rural and suburban prehospital settings. It is a convenient approach that can be safely implemented by BLS-EMT with the support of an online medical control center. In this study, SC administration yielded a very low rate of adverse effects and vital signs abnormalities during prehospital transport. Our results indicate that the protocol is effective for pain management, but further prospective studies are needed to confirm effectiveness and to determine the benefits and limitations of this novel approach to pain relief.

References