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BUPRENORPHINE FIELD INITIATION OF ReSCUE TREATMENT BY EMERGENCY MEDICAL SERVICES (BUPE FIRST EMS): A CASE SERIES

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ABSTRACT

The opioid epidemic is currently a leading health crisis in the United States, and evidence supports Medication for Opioid Use Disorder (MOUD) as the most effective treatment (2). In our EMS system we are observing an ever increasing number of patients who, due to refusing transport after naloxone rescue, represent an access void at the point of overdose. We present a case series to illustrate a new treatment paradigm utilizing front line EMS paramedic units and high dose buprenorphine to treat withdrawal symptoms with next day bridge to long term care. The three patients described are exemplary cases, meant to represent overall characteristics of the intervention prior to complete data collection. Each patient was revived from opioid overdose with naloxone. Paramedics then treated each patient with 16 mg of buprenorphine to relieve and prevent withdrawal symptoms. Patients were provided with outpatient follow up irrespective of ED transport. To the best of our knowledge, this is the first EMS agency in the United States providing MOUD in the prehospital setting at the point of overdose. This innovative program provides EMS with education and tools to promote patient engagement. While still in its infancy, this approach utilizes existing EMS resources to bring MOUD to the prehospital setting, offering a new avenue to long term care. **Keywords:** Opioid, buprenorphine, emergency medical services, medication assisted therapy, naloxone, overdose

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BACKGROUND

Opioid overdose continues to be the leading cause of preventable death in the United States. In 2017,

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68% of the 70,000 overdoses nationally were opioid-related; an increase of 9.6% from 2016 (1). Historically, treatment for opioid use disorder (OUD) focused on detoxification and rehabilitation services, but evidence now clearly points to pharmacotherapy as the most effective treatment modality(2). Despite efforts to increase delivery of evidence-based care across the United States, approximately 1.7 million people are still not engaged in treatment (3).

In response to the opioid crisis, our inner-city, university hospital created a Medication for Opioid Use Disorder (MOUD) program. This includes an Emergency Department (ED) staffed with X-waivered Emergency Physicians who initiate MOUD with buprenorphine and link patients to outpatient care. Buprenorphine, a partial opioid agonist with high receptor affinity and FDA approval for MOUD, is effective for treatment of withdrawal and linkage to care(4). Unfortunately, EMS transport refusals after naloxone administration in our system increased from 2% in 2016 to 36% in 2019, creating a patient access void in our ED MOUD system.

While naloxone is an effective antidote to the respiratory toxicity of opioids, it is known to cause withdrawal symptoms when reversing toxic effects. Careful dosing of naloxone may help in minimizing precipitated withdrawal, however multiple barriers exist to preventing over utilization of naloxone. First, there are multiple entities who may be administering naloxone to patients prior to EMS arrival, including police or bystanders. In addition, intranasal naloxone, which is the standard for police, bystanders, and EMTs, is not easily titratable. Often patients receive large doses and are already in withdrawal prior to contact with EMS, furthering the potential for a refusal of transport to the ED for linkage to treatment.

As such, our institution's Emergency Medical Services (EMS) and Addiction Medicine divisions partnered to create a program with EMS initiating MOUD and serving as a bridge to definitive care. The program developed in three parts: EMS provider OUD education to increase patient engagement; a patient-centered, harm-reduction package that includes emergency naloxone, a list of needle

exchanges, and patient treatment resources; and finally, a protocol authorizing paramedics to administer buprenorphine for opioid withdrawal symptoms and provide next day linkage to care, independent of ED transport. Patients who attend their initial appointment and remain engaged receive the benefits of a robust bridge clinic including weekly appointments, buprenorphine maintenance, mental health visits, counseling, and access to social services.

The third prong of our program required legislative action because buprenorphine was not part of the paramedic scope of practice in our state. Partnering with key state officials, we were permitted to make our case for paramedics to add buprenorphine to their treatment options with strict physician oversight. In June 2019, the state released a temporary executive directive allowing buprenorphine administration by paramedics for the purpose of treating withdrawal symptoms and linkage to long term care, thus allowing the program to move forward.

NARRATIVE

Setting

Our EMS system is a hospital-based, two-tiered service primarily utilizing Emergency Medical Technicians (EMTs) and paramedics with additional support from a 24-hour paramedic supervisor response vehicle and EMS physician response units. In 2019, of the 44,466 EMS responses in Camden, 25% were to patients with suspected overdose.

In our initiative, paramedics were offered education on OUD through a combination of lectures, literature review, clinic observation, and counseling training. Additionally they were all trained in the protocol by written and psychomotor testing, and then had direct observation by EMS physicians of field protocol implementation. All paramedics in the program had a minimum of ten education contact hours. This was followed by agency-wide patient engagement and resource dispersal, leading to gradual paramedic unit adoption of our Bupe FIRST EMS protocol.

Protocol

Patients who regain full decisional capacity after an overdose resuscitation that includes naloxone are assessed for on-site MOUD treatment (Figure 1). To qualify for treatment, a patient must have a Clinical Opiate Withdrawal Scale (COWS) score >7 or be opiate-free for 72 hours prior to overdose. Patients

are ineligible if they used methadone in the past 48 hours, are pregnant, younger than 18 years old, or unwilling to provide their name and date of birth for follow up and tracking. Paramedics present the case by phone to an X-waivered direct medical oversight physician familiar with the Bupe FIRST EMS protocol. If approved, paramedics administer 16 mg of sublingual buprenorphine and monitor the patient for an increase or decrease in withdrawal symptoms. Paramedics can administer 4 mg ondansetron for nausea and an additional 8 mg sublingual buprenorphine for patients who do not respond fully to the initial dose. Patients are provided with addiction resources and a clinic appointment the next day. Following treatment, patients may either consent to ED transport or refuse further care.

Case Series

Of the eighteen patients enrolled in Bupe FIRST EMS at the time of this manuscript, all had improvement in symptoms following buprenorphine treatment, without any signs of precipitated withdrawal. Three exemplary cases (Table 1) were selected based on the depth of documentation available and representation of varied patient characteristics, in order to illustrate preliminary results of this intervention.

Patient A: A 29 year old male who was found apneic was administered 2 mg of naloxone intramuscularly. He regained consciousness and demonstrated capacity with documented withdrawal symptoms including a heart rate of 136, dilated pupils, irritability, and anxiety. His initial COWS was 13, indicating moderate opioid withdrawal. Per protocol, paramedics administered 16 mg sublingual buprenorphine. Thirteen minutes after buprenorphine administration, the patient's repeat COWS score was 3. He refused ED transport and was given a clinic appointment for the next day. Total paramedic contact time was thirty-six minutes. The following day the same paramedics met the patient outside the addiction clinic and escorted him to registration; at thirty days, he remained engaged in treatment at the clinic.

Patient B: A 31 year-old male with last known opiate use 16 days prior was found with respiratory depression rapidly followed by apnea and received naloxone 2 mg intramuscularly. He regained consciousness and demonstrated capacity with documented withdrawal symptoms including a heart rate of 150, diaphoresis, dilated pupils, nausea, irritability, and anxiety. His initial COWS was 15, indicating moderate opioid withdrawal. Per protocol, paramedics administered 16 mg sublingual buprenorphine. He proceeded to immediately vomit the

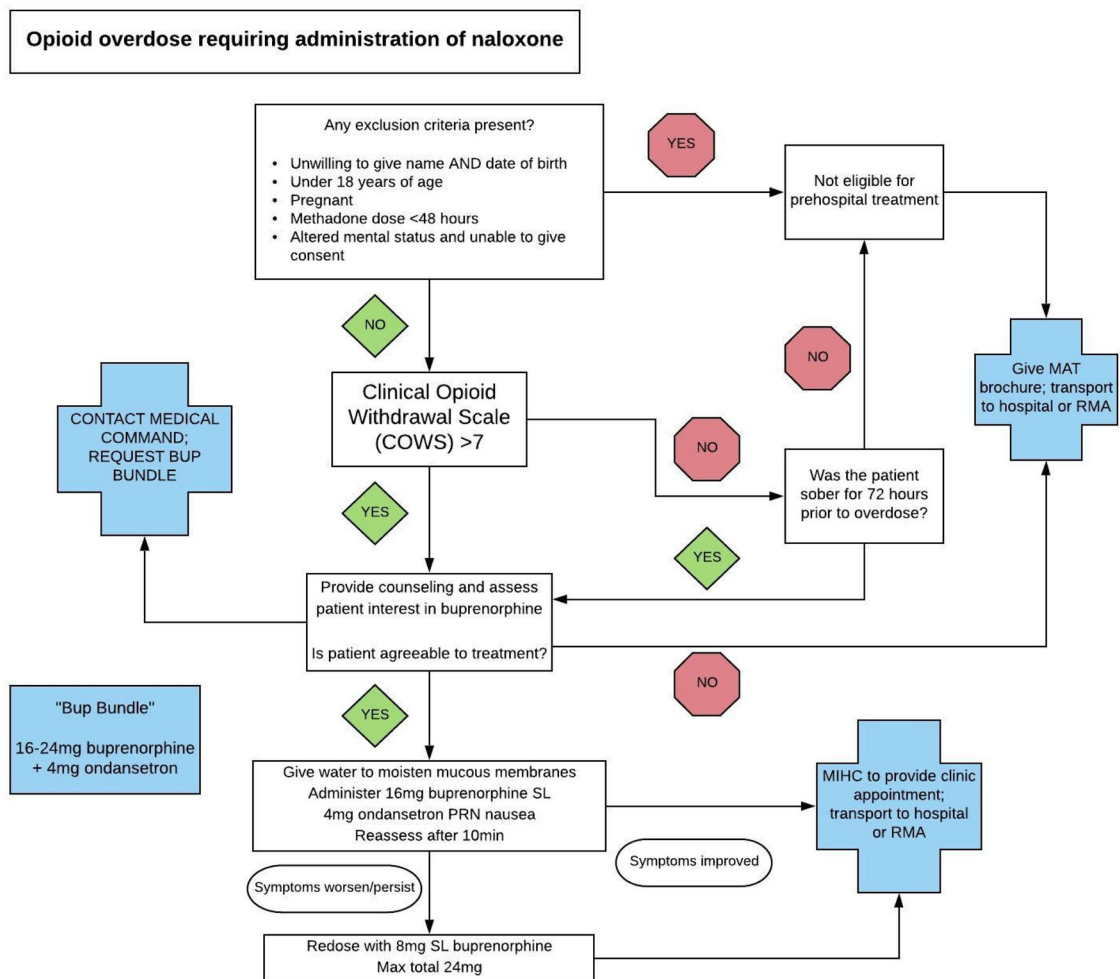


FIGURE 1. Bupe FIRST EMS Protocol.

TABLE 1. Patient Characteristics and Treatment

Patient	Naloxone given	Initial COWS	Buprenorphine given	Repeat COWS	1 st visit	30 day retention
A	2 mg IM	13	16 mg	3	Yes	Yes
B	2mg IM	15	16-32mg	3	Yes	No
C	4mg IN	12	16mg	4	Yes	Yes

medication and 4 mg of intramuscular ondansetron was administered. His repeat COWS was 16 and paramedics, with repeat authorization, again administered 16 mg of buprenorphine. Eight minutes later his COWS was 3. The patient was scheduled for a clinic appointment the following day and was transported to the ED. Total paramedic contact time was 35 minutes. The patient attended his next day clinic appointment; at thirty days he did not remain engaged in treatment at the clinic.

Patient C: A 45-year-old female was found apneic and given 4 mg intranasal naloxone by police prior

to EMS arrival. She regained consciousness and demonstrated capacity with documented withdrawal symptoms including a heart rate of 140, diaphoresis, dilated pupils, and irritability. Her initial COWS was 12, indicating moderate opioid withdrawal. Per protocol, paramedics administered 16 mg buprenorphine films sublingually. Ten minutes later, her repeat COWS was 4. The patient was scheduled for a clinic appointment the following day and was transported to the ED. Total paramedic unit contact time was 31 minutes. The following day, the same paramedics met the patient

outside the addiction clinic and escorted her to registration; at thirty days she remained engaged in treatment at the clinic.

DISCUSSION

Studies have demonstrated the efficacy of buprenorphine in reducing mortality in patients with OUD (2, 5). However, there remain access barriers to medication-based care. In our service area, this is especially true of a subgroup of patients that increasingly refuse transport after overdose reversal. Our EMS service has become this group's primary access to the healthcare system. Without access to longitudinal care resources, patients seem to face a seemingly hopeless cycle of overdose and complications, frequently leading to death. This cycle may also contribute to despondency and compassion fatigue among all levels of healthcare providers. Given the existing infrastructure in this healthcare system, which includes a buprenorphine-prescribing ED and a network of outpatient providers, an innovative approach utilizing EMS was created aimed at field initiation of MOUD, with the goal of empowering EMS with education and tools to promote patient engagement as well as a possible antidote to the compassion fatigue and burnout experienced by prehospital providers.

This program adapted a time intensive, outpatient based induction protocol to field use where operational scene time had to be minimized. Within these constraints, EMS needed to treat withdrawal, engage this vulnerable population, and translate this contact into a long term treatment opportunity. This was accomplished by combining the standard gradual titration doses of buprenorphine into a loading dose of 16mg, rapidly treating withdrawal symptoms. We found that on average our on-scene time increased by only ten minutes for patients enrolled in Bupe FIRST EMS, an acceptable time increase in our high volume, high unit hour utilization system given the potential benefits of treatment.

While precipitated withdrawal is a concern with early induction of buprenorphine, we have found that using larger doses of the medication while patients are exhibiting signs and symptoms of withdrawal appears to alleviate rather than worsen symptoms. Buprenorphine exhibits a high affinity for mu-opioid receptors. In vitro, its affinity for mu-opioid receptors is five times higher than morphine and six times higher than naloxone (6); it is also significantly longer acting (7). High doses of 16mg result in 90-95% receptor binding and when used in inductions, increase patient retention (8, 9). High doses may result in increased receptor saturation

with only partial agonism, providing a cumulative opioid effect preventing precipitated withdrawal. Based on this data, we theorized that using a larger initial dose for induction would be safe for patients and bypass any precipitated withdrawal, improving symptoms in a single dose without requiring time intensive titration. In our limited experience thus far, a single large dose appears to bypass the precipitated withdrawal described in the literature (10).

The benefits of medication assisted therapy for OUD have been well described, with research showing that it is the only intervention that decreases mortality (11). However, barriers to these programs include availability of clinics and providers, as well as patient access to these resources. This is especially noted in our population, given the high percentage of undomiciled and uninsured patients who we encounter with OUD. As the healthcare system matures, traditional roles are being challenged and systems are trialing novel ways to engage at-risk populations. For EMS, the traditional binary transport from scene to ED may not be patient-centered, nor cost effective. EMS systems across the country are inventing new ways to leverage EMS in order to meet healthcare system voids (12, 13). This program expands upon this model, empowering EMS with traditionally office or hospital-based MOUD treatment at the point of overdose, irrespective of ED transport.

As a case series, many limitations exist to generalizing the data presented. Our initial numbers are small, and will require significant increase in order to evaluate for both advantageous effects of treatment and any adverse outcomes. In the future, a statistically robust study will be required to determine the effectiveness of the program. These initial, exemplary cases are illustrative of our current program, and may inform others who are innovating similar EMS responses to OUD. While still in its infancy, this innovative approach utilizes existing EMS resources to bring MOUD to the prehospital setting, offering an at risk population with a new avenue to long term care.

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